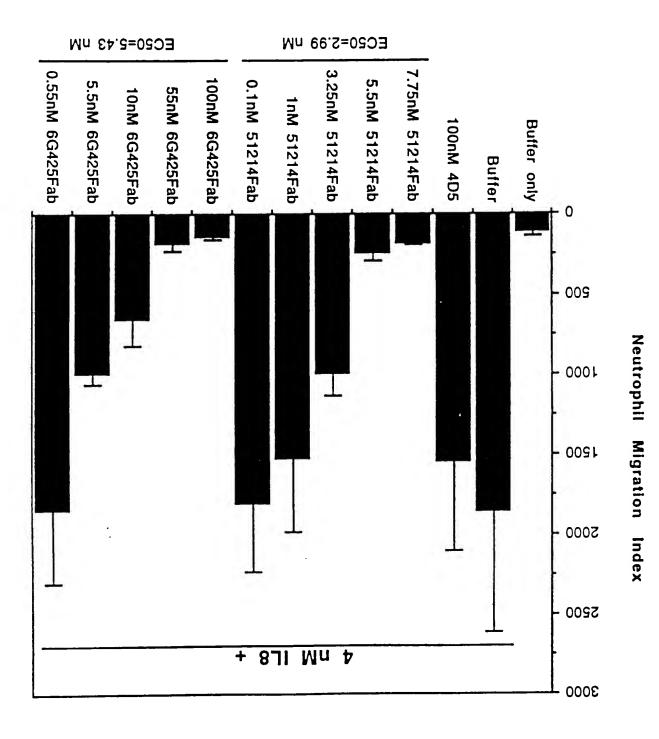
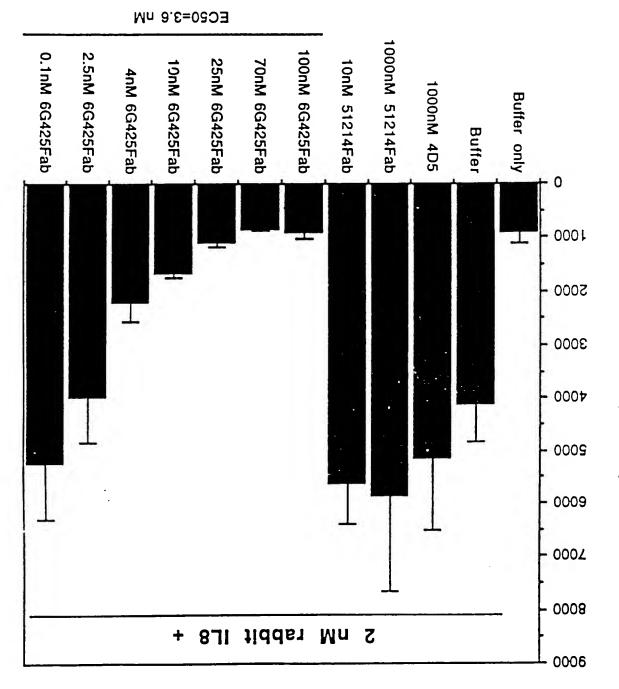
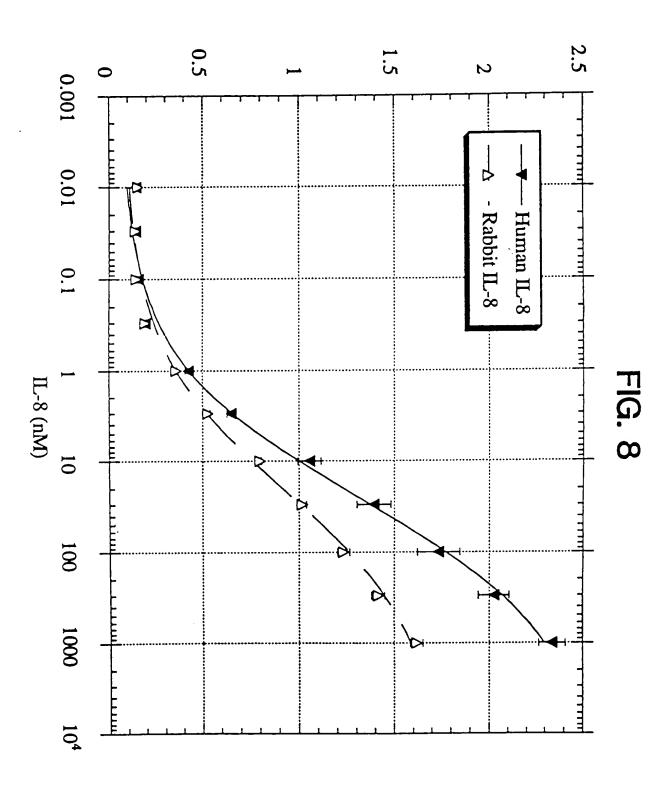


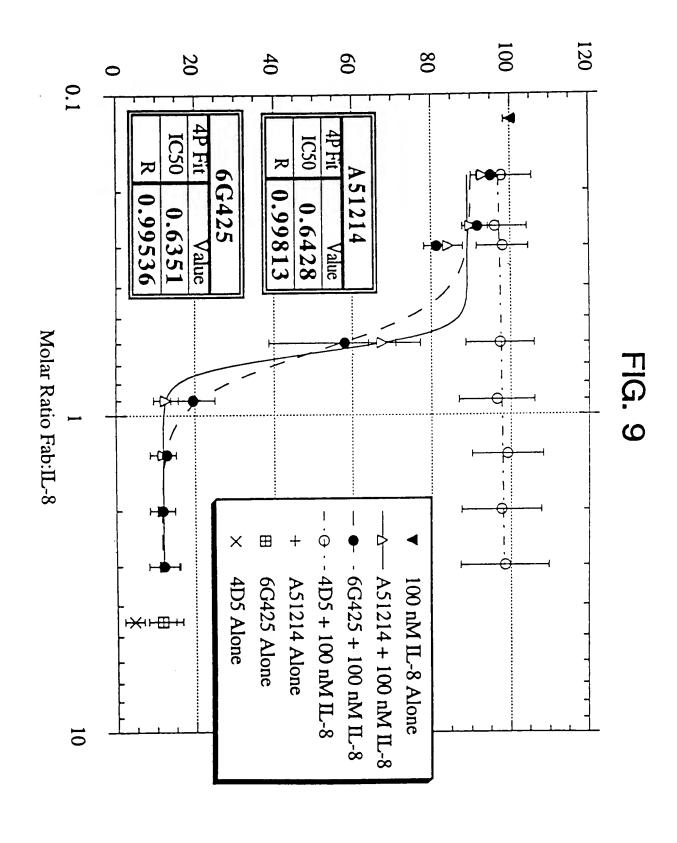
FIG. 6

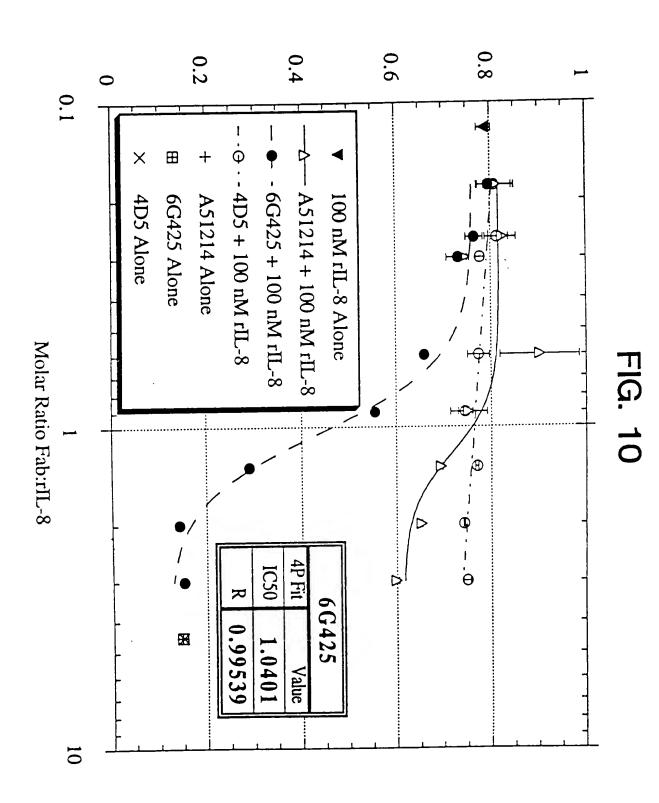


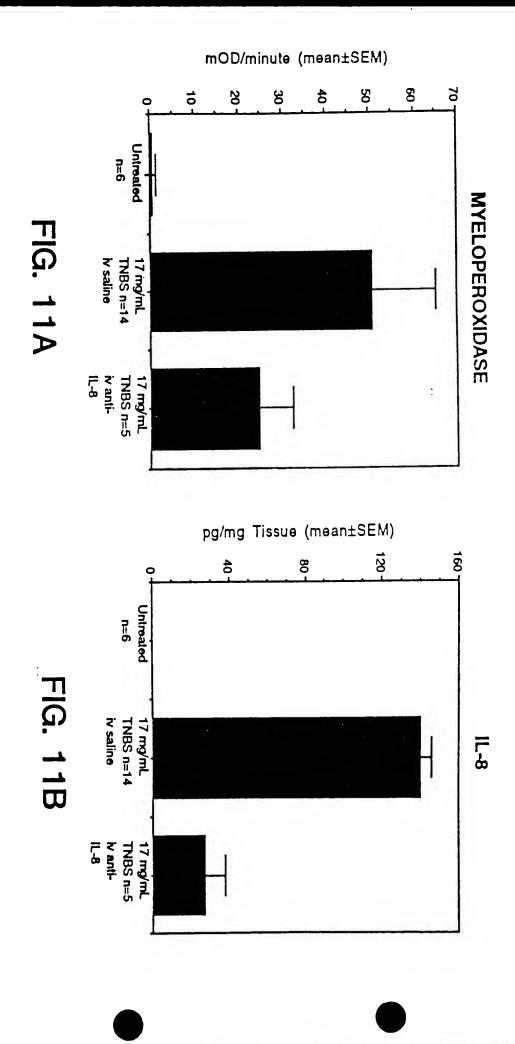


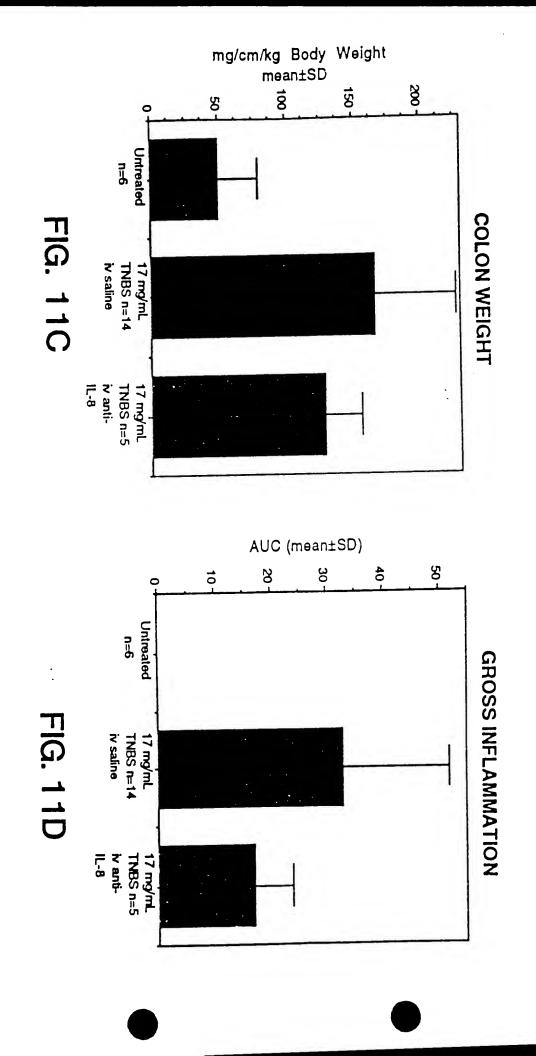
Neutrophil Migration Index

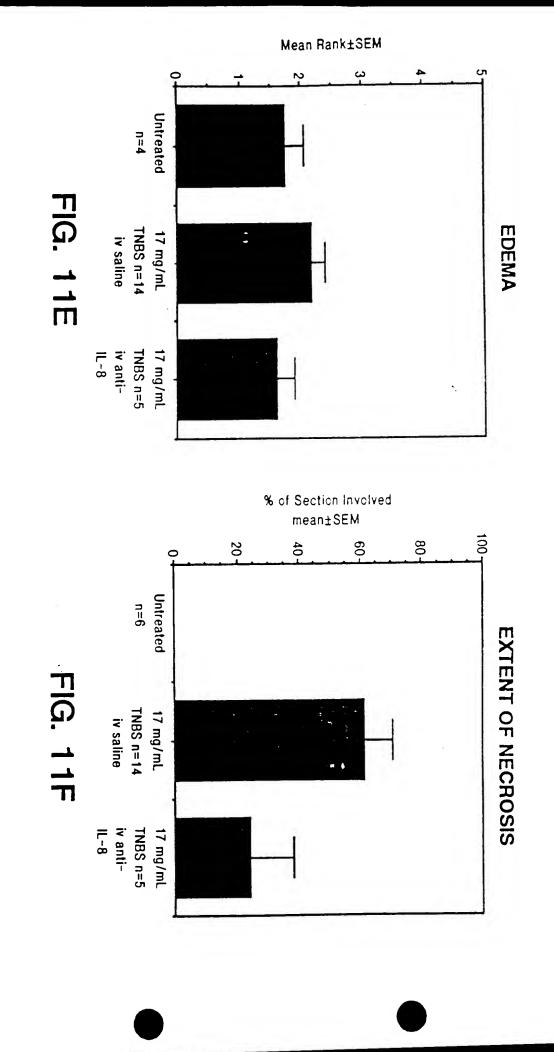


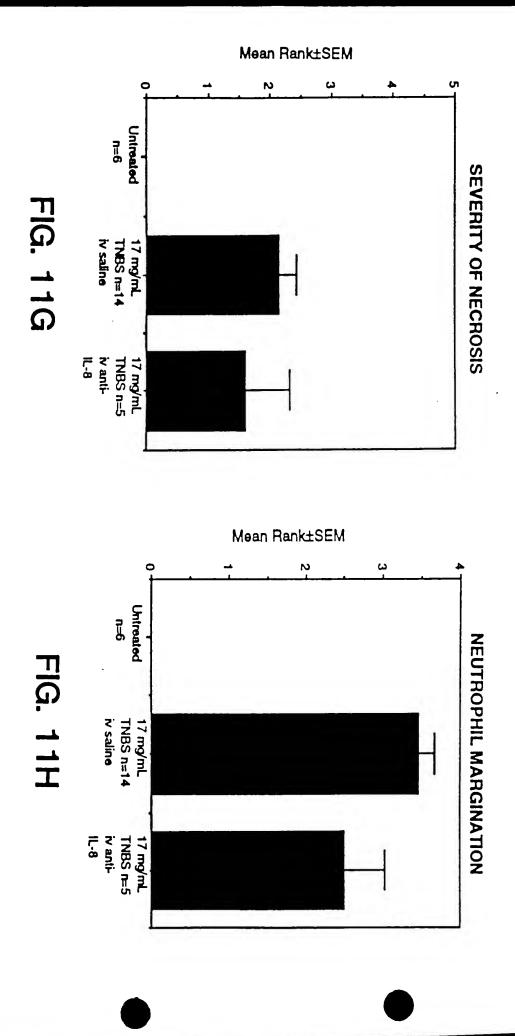


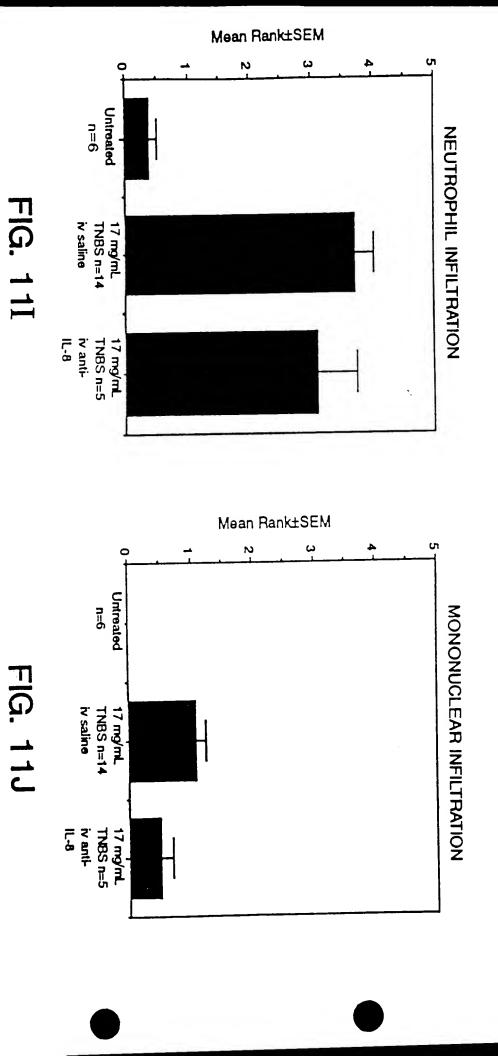


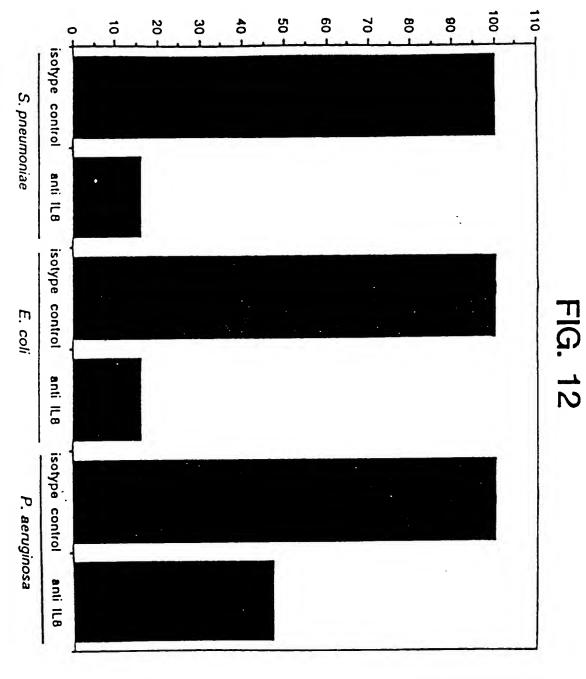












Neutrophil emigration index (%)

Group (n=5 rabbits per group)

Light Chain Primers:

WKTC-J' SSWGE **EIG' 13**

' E DOBOABBAOTTBTOAAOOTBAO ' 2

WKTC-Z' ZZWGI

S GTGCTGCTCATGCTGTGC 3'

(SEG ID NO: T)

MKTC-3, 23mer

(E:34 QI 432) 'E DODTOTOTOTOTADTTOAAD 'Z

Heavy Chain Primers:

IGGSÝG-I' S∉wer

5' GCATCCTAGAGTCACCGAGGAGCC 3' (SEB ID NO: 4)

IGGSAC-2, S2mer

IGGSAC-3, 22mer

S GGAGAGGTGTGCAC 3' (SE& 10 NU: 6)

(b:01 (5 435)

(3:007:73)

(人):河下短约

A

Light chain forward primer

SL001A-2 35 mer

SPOOTE 37 mer

'E STASSSAGTASTASAG TSGSATGSGSAAASA 'E T T T

Light chain reverse primer

FIG. 15 Heavy chain forward primer

S CGATGGGCCCGG ATAGACCGATGGGGCTGTTGTTGGC 3 'S

STOOSE 39 mer

A Ð

Heavy chain reverse primer

39-MER STOOSE

 \mathbf{T} 5. CGATGGGCCCGG ATAGACCGATGGGCTGTTTTTGGC 3. (SELTORS)

Ð A

H: 201 (II 735)

(2日11113)

51:74 (1 975)

(41:01 (I 1935)

E1:2.4(1735)

(21:0N OI 935)

(11:0711730)

	FIG. 16	771		(269 ZO NO: 19)	BStBI 361 CCATTCGAA GGTAAGCTT 121 P F E
CATCTTCCCA GTAGAAGGGT I F P	CAACTGTATC GTTGACATAG $T V S$	GCTGCACCAC CGACGTGGTG A A P P	ACGGGCTGAT TGCCCGACTA R A D	TGGAGTTGAA ACCTCAACTT E L K	301 GGGACCAAGC CCCTGGTTCG 101 G T K L
GTTCGGTCCT CAAGCCAGGA F G P	ATCCTCTCAC TAGGAGAGTG PLT * * *	TATAACATCT ATATTGTAGA Y N I Y * * * *	CTGTCAGCAA GACAGTCGTT C Q Q * * CDR	CAGACTATTT GTCTGATAAA D Y F	241 GAAGACTTGG CTTCTGAACC 81 E D L A
TGTGCAGTCT ACACGTCAGA V Q S	CCATCAGCCA GGTAGTCGGT I S H	TTCACTCTCA AAGTGAGAGT F T L T	TGGGACAGAT ACCCTGTCTA G T D	GCAGTGGATC CGTCACCTAG S G S	181 CGCTTCACAG GCGAAGTGTC 61 R F T G
AGTCCCTGAT TCAGGGACTA V P D	GGTACAGTGG CCATGTCACC Y S G	TCATCCTACC AGTAGGATGG S S Y R * * * *	GATTTACTCG CTAAATGAGC I Y S	CTAAAGCACT GATTTCGTGA K A L	121 GGGCAATCTC CCCGTTAGAG 41 G Q S P
ACAGAAACCA TGTCTTTGGT Q K P	CCTGGTATCA GGACCATAGT W Y Q	ACTAATGTAG TGATTACATC T N V A * * * *	GAATGTGGGT CTTACACCCA N V G CDR #1	AGGCCAGTCA TCCGGTCAGT A S 0	61 GTCACCTGCA CAGTGGACGT 21 V T C K
CAGGGTCAGC GTCCCAGTCG R V S	CAGTAGGAGA GTCATCCTCT V G D	ATGTCCACAT TACAGGTGTA M S T S	TCAAAAATTC AGTTTTTAAG Q K F	TGACACAGTC ACTGTGTCAG T Q S	1 GACATTGTCA CTGTAACAGT 1 D I V M

	71 '9I=	1	(61:0N OI 735)	JJJ55AT 4	130
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	GGTAGACAGA Y V Z q	A T T	A A A	CAGTGACAGA	TCCCTGAGAC T T D	113
	TOTOTOTACO	DODADAADAA	AASSEASSTS	TOTOTOAOTO	PECTOTO	198
		E# AC	CI			
M C Ö	* * * * M E G X	T A 2	* * * S I 7	A A A D	M F Y	٤6
ADDDDDDTDA TDDDDDDDADT	TTSSTTTSST AASSAASSA	TOATOBBOTT ADTABOODAA	DATTACTCCC CTAATDACCC	DADAADDTÖT DTDTTDDADA	DATTTTDTAD	301
A T G	CACTTCAGAC	S S W	X P G	K N T L	D N A	٤٧
DDADADADDA DDTDTDTDTDT	DTDTDAADTD DADADTTDAD	TOADDADTAA	ADDTDDATDT	OOOAOAADAA	SSETAASASA	241
			7	CDK #3		
A S I	тяяр	* * * 2 A K	* * * X b D	Y T Z Q		٤٤
DOOOTOTAOO DDDDADATOO	AOTTABOODD TBAATODDOO	DAADTDTDAD DTTDADADTD	ADADOTATTA TOTODATAAT	TOOADDATAD ADDTDOTATO	TOOTAATAAT AOOATTATTA	TBT
* * *	E r A y	K Z P	5 d Т	млкб	* * * S W D	33
AATTADDAAD TTAATDDTTD N I T	DOTESTTEAS DEADOAAOTO	CTTCTCGA	CTCAGGTCT	ACCCAAGCGG	ADADATDDDA	ısı
	CDK #					
* * X S S	<u> </u>	S A A	r a c	c a r k		13
ATTÐATÐAÐT TAAÐTAÐTÐA	TATACTTAEE ATATEAATCC	TOTOODAODT ADADOOTOOA	DTOCTOTAA OADDADADTT	A5T333T555 T3A555A333	A99T009009 T00A990990	τ9
G r A	D D S E	o r v	E A			τ
<u> </u>	SSS SS	-2422493193	ADDIDABDET	TOOOOAAAOA	TOOTTATOTT	τ

(EZ:07/6]:735) .E	Ð	TOADADADOTODADOTODIT <u>OOODD</u> TAD 'Z
		VH.rear 33-MER
(22:27 0 5 7 3 5)	، ٤	5 CCACTAGTACGCAAGTTCACG
		VH.front.SPE 21-MER
(12:00 (FE DES)	٤	DDTTODAOOTODAAQOTTOTAODAOO
		VL.rear 31-MER
(22:174 (1) 1935)	٤،	DADADTADTOTATADTODDATDODDAAAOA ' 2
		VL.front 31-MER

FIG. 19 (45:0101,532) AATT TIL 198 H Q G L S S P V T K S F N R G E C (SELTOID: 25) DADITIODDO TETTEAABOT DITTTETEADE DEDEABOTOA DEDOCUTEATE 661 CATCAGGGC TGAGGTCGCC CGTCACAAG AGCTTCAACA GGGGAGAGTG IJ8 I T I Z K Y D X E K H K A X Y C E A I DETECTOR OF TOTAL STATEMENT STATEMENT SOLUTION OF THE STATEMENT ST COACTEACEC TEACHARD SALASARA DABOATCADA CERARDORET COCAGETCOCA 103 ISS T S A L S Q X S Q O E L A S E O S N 85I DOTEOTOR DE L'ADELLE TOTOTTOL DE L'ADELLE COLOR DE L'ADELLE COLOR DE L'ADELLE COLOR DE L'ADELLE L'ADEL SAI AACTCCCAGG AGAGTGTCAC AGAGCAGGAC AGCAAGACA GCACCTACAG CCTCAGCAGC 138 N L X B K E Y K A O M K A D N Y F O S C ADDDATTOD ADDDDDTTAT DOADDTTDOA DITACTTO DODDTDTDD DATABAADTT TISE PPS DEQ LAS GTAS V U L L ATTOADOADO DADADADAD AADDADTTDD ABATTTDAAD TDDTDATDAD ATDDDDDDAA TAASTOSTO STETETTOTO TTOSTOADS TOTAASTTS ASSASTABLY TASSESSORT ISA 98 F G P G T K L E L R R A A A A P S V F I DATABADAD DATABATOT CTCABATOT TODAADOTOO ADOTTODAD OADDADODAA BSEBI CDK #3 78 V Q S E D L A D Y F C Q Q X N I X DETEABABEA TABATETTAT ATTECTEADA DAAATAETST ESSAASTETT SABASTESAS 301 GTGCAGTCTG AAGACTTGGC AGACTATTTC TGTCAGCAAT ATAACATCTA TCCTCTCACG 28 A D B E L G Z G Z C L D E LTLT ATOOCTOATO OTOAOAOTOA AATOTOCOCA AOATOCACTO COLORADO DATOAOODAO TADDADIAD CATTOADT TTABADADED TOTABETEAD EBADADITOE CIAETODOTE IAS CDK #5 38 Ö K b C O S b K Y I I X Z Z Z K K TOCADTATA DESTABATE ADEADTAAAT DASTECTION STEETINGS STEETINGS ASSTSACATE SOCIATORIA TECTOS SECUENTIAN STORES SECUENTIAL STORES SECUENTIAL S CDE #I * * * 18 R V S V T C K A S O N V G T N V A TTDATACCAG DOTACATTAG TACCCCACT OTDACTEDOC TTDCAGGTGA COCTACACT 121 AGGTCAGCG TCACCTGCAA GGCCAGTCAA DATGTGGGTA CATGTAGC CTGGTATAA -3 A S T S M T Q S Q K F M V I G A Y A E-STOTOOTACT DATGEDACA TOAATTTTTD ABACTGTGT ATBACGATAT CABCGTACGC SABABBATBA STASASSTOT ASTTAAAAAS TSTAGASASSTORE ATSBSTATA STSSSATSSS 18 -23 M K K N I Y E P P R M E N E S I STITGIADA ATABAAAAA DAADATADA TADAAAAA AATADAATAT TOTITGITG I ATATATTTTT DOTTATATT ADATATAT TTADADTATA ADAADAADTA I

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TTAA

FIG. 20A

SESTITES AS ESTABLISHED SOLVED IN S	DACCTCCAG CTODAGODOA C C G	OTGGTGACCG CACCACTGGC V T V V	SOMEOTICE	DADTADADTO	542T23T542 103 ST5455A2T5 5 2 2 9 871
ATOOTOTOOO TAOOAOAOOO A V A	<u> </u>	DETECTORS A STATE OF THE A STATE OF	SCGGGACTGG	CCTTGAGTCC	TECTETEENA 112
CGAACCGGTG GCTTGGCCAC F P V	ACTACTTCCC TGAAGAGGG TATA	CTGGTCAAGG GACCAGTTCC L V K D	GGACCCGACG	29929A2A29 92292T9T92	SSSSTOTOOA (8)
CTCCAAGAGC GAGGTTCTCG S K S	OTOOOAODDT DADDDTDOOA 2 4 A	GTCTTCCCCC CACACCCCC CACACCCCCC CACACCCCCCCC	IsqA SOTACCODED DDATDEDCCO	AADDADDTDD TTDDTDDADD	421 GTCTCTGCAG CTGCAGAGAC A A R V 811
		* *	* * *	CDK #3	* * *
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TOAOTEETOT AETEADOAEA	2499944239 9T222TT992	SOSTARTES SOSTARASS	TTTDDTTDAT AAADDAADTA	SSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSS	ADTDDDDADA 18E
X C Y	T M A	AGACTCCTGT T G E D T	2 P K	S M Q	TGGGACATGG
ADDTDTDATT TDDADADTAA	TTSTASSSAS AASATSSSTS	ADADDADTOT	DAADTOTDAO	DADTAAADDT	301 ACCCTGTACC
					CDK #5
и х ч	и о	SILA	* Ксв	* * * D 2 A	4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4
คบบาบบาล		ADATDDTDAA	TODDOOOTTO	ADADTOTO V 2 Q * * *	4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4
* * * * * * * * * * * * * * * * * * *	*	* * TOTACCACTT ADATECTAC	ADOOGGGAAD TODOOCTTO	TOTOACACAC ACACTOTOTO V & G	DTATTATODA IAS TGATAATADA T Y Y Y R
S G D * * * * DAABAASSET STISTEDSA	TTATTATTAA N N A A A A A A A A A A A A	TOTACOCAT T A V T T A V TOTACOCATT ADATOTAA	DAACTCAAC L E L L E L ABOUTTO	Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X Z D Z X	T Q A 8E T Q A 8E T Q A 8E TATATATOTA LAS TATATATATA TATATATATA TATATATATA TATATATATA TATATATATA TATATATATATA TATATATATATA TATATATATATATATATA TA
S G D * * * * DAABAASSET STISTEDSA	TTATTATTAA N N A A A A A A A A A A A A	TOTACOCAT T A V T T A V TOTACOCATT ADATOTAA	DAACTCAAC L E L L E L ABOUTTO	Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X Z D Z X	T Q A 8E 241 ACCTATTATC TGGATAATAG TGGATAG TGGATAG TGGATAATAG TGGATAG TGGATAATAG TGGATAATAG TGGATAATAG TGGATAG TGGATAG TGGATAT
S G D * * * * DAABAASSET STISTEDSA	TTATTATTAA N N A A A A A A A A A A A A	TOTACOCAT T A V T T A V TOTACOCATT ADATOTAA	DAACTCAAC L E L L E L ABOUTTO	Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X D Z X Z D Z X	T Q A 8E T Q A 8E T Q A 8E TATATATOTA LAS TATATATATA TATATATATA TATATATATA TATATATATA TATATATATA TATATATATATA TATATATATATA TATATATATATATATATA TA
DATADTOT DOTATOACOA S G D TABLES T	AATAATAATT AATTATTAA TTATTAAA N N N AACAGAGACCC AACAGACCCC TTOTOTOTOTOTOTOTOTOTOTOTOTOTOTOTOTO	# ADDACOR # I CACCAACCA CACCATCA CACCAT	S G F F TOTAGAGTTG TOTAGAGTTG TOTAGAGGGGGGA TOTAGGGGGGGA TOTAGGGGGGGA TOTAGGGGGGA TOTAGGGGGGA TOTAGGGGGGA TOTAGGGGGGA TOTAGGGGGGA TOTAGGGGGGA TOTAGGGGGGA TOTAGGGGGGA TOTAGGGGGGA TOTAGGGGGGGA TOTAGGGGGGA TOTAGGGGGGGA TOTAGGGGGGGGA TOTAGGGGGGGA TOTAGGGGGGGGA TOTAGGGGGGGGA TOTAGGGGGGGGA TOTAGGGGGGGGA TOTAGGGGGGGGA TOTAGGGGGGGGA TOTAGGGGGGGGA TOTAGGGGGGGGA TOTAGGGGGGGGA TOTAGGGGGGGA TOTAGGGGGGGGA TOTAGGGGGGGA TOTAGGGGGGGGA TOTAGGGGGGGGGA TOTAGGGGGGGGGA TOTAGGGGGGGGA TOTAGGGGGGGGGA TOTAGGGGGGGGGA TOTAGGGGGGGGGA TOTAGGGGGGGGGA TOTAGGGGGGGGGA TOTAGGGGGGGGGA TOTAGGGGGGGGGG	A A D CAGGCAAGAG CAGGCAAGAG CAGGCAAGAG CAGGCAAGAG CAGGCAAGAG A A A A A A A A A A A A A A A A A	18 L K L S TGCCAGACTC GCGCTCTGAG TGATATATC TGGATAATAG T
V W Z DATABTEET DATATOADOT R R R R S G D AABAADOET DAABAADOET DAABAADOET DAABAADOET DAABAADOET DAABAADOET	ATACTAATT AATAATAATT AATAATAATT TTATTATTA	TACTEAATAT 2	a S F F S S S S S S S S S S S S S S S S	A A D CAGGCAAGAG CAGGCAAGAG CACGCAAGAG	18 L K L S TGCCAGACTC GCGCTCTGAG TGATATATC TGGATAATAG T
TTOOOTTOTO AAOOOAAAAO V W Z OOTATOAOOT S U D TTOTOAO	TADDOTATTO ATDODATAAD A D X A D X ATAATAATT AATAATTAA TTATTAATTAA N N N AADADADODO	TATACAGTA TATACAGTA TATACAGTA TATACAGTA CDR #1 CTCCCAACCA CACCATCA TATACAGTA TATACAGT	V E S CTCTGGATTC GAGACCTAAG S G F CCTGGAGTTG GGACCTCAAC L E L L E L GAAGGGCCGA GAAGGGCCGA CTCCGGCTTC CTCCGGCTTC CTCCGGCTTC CTCTGGAGTTC CTCTGGAGTTC CTCTGGATTC CTCTGATTC CTCTTT CTCTGATTC CTCTTT CTCTTT CTCTTT CTCTTT CTCTTT CTCTTT CTCTTT CTCTTT CTCTT	V Q L CCTGTGCAGG GACACGTGG A A C CAGGCAAGAG CTCTCTCTC CACGCCACAGAG CACGCCACAGAG CACGCCACAGAG CACGCCACAGAG CACGCCACAGAG CACGCCACAGAGAGAG	121 CTGAAACTCT GACTTTGAGA 121 CGCCAGACTC GCGGTCTGAG 38 R Q T P GCGGTCTGAG TGGATAATAC TGG
E DE SERVICION SE DE SERVICION	TACCOTATA A D X	A DO TODO O O O O O O O O O O O O O O O O	CCACCTCAGA V E S CTCTGGATTC GAGACCTAAG S G F CCTGGAGTTG GGACCTCAAC GGACCTCAAC GGACCTCAAC GGACCTCAAC CTGGAGGCCGA	TCACGTCGA U Q L V Q L CCTGTGCAGC GACACGTCG CACGCCAAGA CACGCC	121 CTGAAACTCT GACTTTGAGA 121 CGCCAGACTC GCGGTCTGAG 38 R Q T P GCGGTCTGAG TGGATAATAC TGG
20T252A25T 20A202T20A 2 0 0 2 0 0 TT352T70T3 AA000A40A0 20TAT0A00A 2 0 0 0 2 0 0 0 0	T S 4 COCOCCO COCCCO COCCC COCC COCCC COCC COCCC COCC COCC COCC COCCC COCC COC	TOPOGOGO TOPOGO TOPOGOGO TOPOGO TOPOGOGO TOPOGOGO TOPOGOGO TOPOGOGO TOPOGOGO TOPOGOGO TOPOGO TOPOGOGO TOPOGO TOPOGOGO TO	L L A GETGGAGTCT CCACCTCAGA TCTCGGATTC GAGGCCTAAG GGACCTCAAC L E L L E L GAAGGGCCGA GAAGGGCCGA GAAGGGCCGA CTTCCCGGCT GAAGGGCCGA CTTCCCGGCT CTTCCCGGCT CTTCCCGGCT CTTCCCGGCT CTTCCCGGCT CTTCCCGGCT CTTCCCGGCT CTTCCCCGCCT CTTCCCCCCCC	A A I ACTGCACCT ACCTCACCA A Q V L Q V COTGTCACCA COTGTCACCA A A D CACCCAACA CACCAACA CACCCAACA CACCAACA CACCCAACA CACCAACA CACCCAACA CACCCA	61 GCGTACGCTG CGCATGCGAC CGCATGCGAC CGCATGCGAC CTCAAAACTCT CACAAACTCT CACAAACTCT CACAAACTCT CACAAACTCT CACAAAACTCT CACAAAACTCT CACAAAACTCT CACAAAACTCT CACAAAACTCT CACAAAAACTCT CACAAAAACTCT CACAAAAAAAA

FIG. 20B

121 GTTGAGCCCA AATCTTGTGA CAAAACTCAC ACATGA (SEW IO NO: 26) CAACTCGGGT TTAGAACACT GTTTTGAGTG TGTACT (SEW IO NO: 26)

661 ACCCAGACCT ACATCTGCAA CGTGAATCAC AAGCCCAGCA ACACCAAGGT GGACAAGAA TGGGGTTCCA TGGGGTTCCA TGGGTTCCA TGGGTTCA TGGGTTCCA TGGGTTCCA TGGGTTCCA TGGGTTCCA TGGGTTCCA TGGGTTCCA TGGGTTCCA TGGGTTCA TGGGTTCCA TGGGTTCCA TGGGTTCCA TGGGTTCCA TGGGTTCA TGGGTTCCA TGGGTTCA TGGGTTCCA TGGGTTCA TGGGTTCCA TGGGTTCCA TGGGTTCCA TGGGTTCCA TGGGTTCCA TGGGTTCCA TGGGTTCCA TGGGTTCA TGGGTTCA

(SEC ID NO: B)		'E DADDTDTDDAADDTDDADADDD 'Z
		IGGSAC-3, S2mer
(5:00 01 735)		S ' CACTGGCTCAGGGAAATAACCC 3
		IGGSAC-2, 22mer
(#:27 OI (935)	٤ ،	S CATCCTAGAGTCACCGAGGAGCC
(IGG2AC-1, 24mer
		Heavy Chain Primers:
(E:27 OI 735)	٤٠	S CAAGTTGTTGTTGAAG
		MKPC-3, 23mer
(Z:24 J. 035)		'E DETECTECTETATOETOETE 'E
		MKTC-Z' ZZWGŁ
: (T:01/0I 035)		' E DOBOABBAOTTBTOAADOTDAD ' Z
•		MKPC-1, ZZmer
		Light Chain Primers:

SEM-DE LEW. Jable 1864. See Action 1864.

Light chain forward primer

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(El : 27/ (JZ 235)
                                          C
                                          A
(H 994 Ot 725)
(SI 984 OL 826)
                                          T
                S: CGATGGGCCCGG ATAGACCGATGGGGCTGTTTTGGC
(11:27 52 935) 18
                                                             SLOOZB
                                                     39-MER
                                      Heavy chain reverse primer
(EL:71 7= 735)
                                       \mathbf{T}
                 5' CAAACGCGTACGT GAG ATC CAG CTG CAG CAG
(रह ३३४ १६ १३५९)
              ۱ ٤
                                            6G4.heavy.Mlu 32-MER
                                      Heavy chain forward primer
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(HE: ON OI 735)	InuM AƏTTAAƏDAÐ	TĐADOTADDA	OOOTTOTAOO	TATOTOAAOO	124
			*	* * * *	
K K Y D Y Y	K r E r	T D A	TFG		86
TOCADOATOA DOCUMENTA	DOTOOADOTT	DDTDDDADDA	DODAADDTDA	DODDAADATD	
ADDIDOTADT DEBODAAADT	DDADDTDDAA	COASSETCE	DODITIONARY	DDDDTTDTAD	198
CDK #3					
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AGGACTIANTE TANATUADDA	DOTTTDDADA	OTDDOOTDDO	TTOTDOADDT	ADDAATOTAA	
COTTTDAAAC ATCTABTCCT	DDAAADDTDT	бссьбессьб	AADADDTDDA	TƏƏTTAƏATT	181
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	I & qA >>>>>>>>TAT >>>>>>>>>>>>>>>>>>>>>>>>>	T STEESTASSS A DASSEATERE) DOADADDDAA DOTOTODDTT	AASSESSITSS	TOTO	BstE	421
	IsaA		9	CDK #			
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L L D	A D W		срм	И Х И	D X	• -	86
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w	I V A	s a a s	LIS	я п н	ΛΝ	A T	87
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	CDK #5						
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STIRCCACTT	ANTERNA TON	4 TOTADDDAA'I	r DDADTDAABB	TACCTTTCTC	ಎಎ ೨೩೨	TTCGT	
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		CDK #Į					
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	s & a	M K b	G B E I	5 5	ı ğ ıov∀		τ
J T	ADTTDDDDDT (OODAADTADT :	DOADTOOADD T DOTOADDTOO A	OTDADDADD T	SOASTI	'ADA D	0 <i>L</i>

- S: CTTGGTGGAGGAGGAGAGAGGTG 3: (SE& ION: 58) SYN. Apa 22 MER
- 5' GTCACCGTCT CCTCCGCCTC CACCAAGGGC C 3' (SE& 3C NC: 40)
- SYN. Bstell 31 MER
- (PERAGE AS) 'E DOTTOTADITATOTADOADDADADEDDADADAD 'E DZ\AE 38WEK

Mutagenesis Primer for 6G425VL

5 (SE NO OT MAS) 'E DOADADDDDDDDDDDDTDDTTD 'E

		A7S	FIG. ?		
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SGACAGCACC SCTGTGTGTGT T 2 T	TTOTTOTO	T DOTOTOTOAC	ASTSTSST	GCCCATTGAG	TAACCTCCAAA ATTGGAGGGTAA S Q A A 821
STTATSSASS	TTODADTƏT.	CTCCGGTTTC A	TOTOOOATAO	AASTTATTSA	481 GTGTGCCTGC CACACGGACG 138 V C L L
AASABABBSA V & A	T D Z	CTCGTTAACT 1 E Q L K	ASTEEATEET S S 4	AGTAGAAGGG T F P	IIS b L A E
TODADDAADA	CTTTGCCCG ?	TTCGACCTCG !	DOTOCOADOA	DODAADDTDA	361 CATGTTCCGC 5055AA7AT5 507 M 86 * * * *
5# ਸ਼	CD				
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ASASTTTABA TSTSAAATST T	STSSSTBATS	DADTDDDADT	DAADOTOTOT	000T0000T0 000A0000A0 q V 0	TATCGCGATTTT TCGCTAAAA B A R B S A A N 82 A A R F S
DDAAADTTTD	TADATDADDA	DOTITIODADA	CGGTCCGGTC	TTOTOOADOT	TDDTTADATT 181 ADDAATDTAA Y W H J 85 * *
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661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCGGGCAGT GTTTCTCGAA GTTGTCCCCT 198 A C E V T H Q G L S S P V T K S F N R G

121 GAGTGTTAA (SEQ LD NO: 41) CTCACAATT 218 E C O (SEQ LO NO: 42.) FIG. 27B

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		A82	_			
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AADDDDDTTD , TTDDDDDAAD '	ATOAĐĐAAOT TAĐTOOTTĐA	95T005T099 00A990A900	PTCCCBCCA PTCCCA PTCCA PTCCCA PTCCA PTCCCA PTCCCA PTCCCA PTCCCA PTCCCA PTCCA PTCCCA PTCCCA PTCCA PTCCCA PTCCCA PTCCA P	OA000000TO 0T000000A0	TOOAODADAA	187
s s a	A 1 q	A A S d	T K G	S & S	S V T V	811
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				CDK #3		
	A D W	* * * * * * E E D A	* * * C D M	<u>в х и</u>	<i>n a b -</i>	86
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SOTEDAADAT STETCTAOAD TOAATOTOOO OTTOOOOTTO AATTTOTOOT TOTAADTAOT DANDITION DANGARDTO ADTIADADDO DAADDDAAD TIAAADADDA ADATIDAIDA ILS

TTOADOATTO DAADDATOAA TOTADOOAAT OOAOTOAADO OTOTTTOOAT DOOTOTOOTT 181 AAGCAGAGCC ATGGAAAGAG CCTTGAGTTG ADAGAGGTCCTTC CATGGTGAA

C K Y Z Z Z Z H X W DADDDADTOD ATOTAOTOD TADTOAATDA ATAADDADAA DODTTODADD ATATOTTDAD

TOAADOOODA DOOTTOATOA DOTOADDIOO ABADTDOTOO ABOTTOATOT OABODIAODO

L L A S M F V

STITISTADOA ATABAAAAA SSAASATABA TSSAASAA AATSSATAT TSTITITTSAT I ATGAAAAAA TATOTTTOT TOTTOTATOT TOTATOTATA ABAAAAAATA I

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DISSENDED TACATCACCA ATSACTTACT TATTSSTOTT COSAACSTO TATASAASTO ISI

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CDE #1

198 661 TTGGGCACCC AGACCTACAT CTGCAACGTG AATCACAAGC CCAGCAACAC CAAGGTGGAC 721 AAGAAAGTTG AGCCCAAATC TTGTGACAAA ACTCACACAT GA AACCCGTGGG TCTGGATGTA GACGTTGCAC TTAGTGTTCG GGTCGTTGTG GTTCCACCTG L G T Q T Y I C N V N H K P S N T K V D TTCTTTCAAC TCGGGTTTAG AACACTGTTT TGAGTGTGTA CT (SEQ ID NO: 43)

FIG. 28B

CDK

THTO

(SER SO NO: 44)

Variable Light Chain Domain

* *	*** * * *		# 1	888. X 88 8 8	
(1-1:02/F 935) 1909MACH	TAVYYCAARGDYRYNGDWI	KALLYLÖMASLRAED	EKCKELIZKDNE	CAIDEZNCELLANÖK	F(ab)-1
FFDVWGQCT (SEB 2) NO: HA)		*** ***** **	* *** **		
(\$4:31 31 035) TO ADWOMEN	24411 CAAAAA	UUSTUSSUHVNATZZ:	EKCKATLTVDT	CKIDEZNCELLKNÖK	9C472
(\$7:21 07 032) TO 40W/033	001 TOO	80 abc	04	20 a	
` 011	007 06	544 00	02		
		TH			

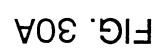
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(14:01 01 93)	RNEYPLTEGOGTKVEIKR	COLYXTATGER 122	17.1730702020	24926/1724 142024	12.00.14
	7 7 7 7	F		n n n n n	
(44:24 9I 035)	# # # ZTHVPLTFGQGTKVEIKR	SSLQPEDFATYYCSQ	GSGSGTDFTLTI	XKVSNRFSGVPSRFS	F(ab)-1
(77, 1 = 1= 7	4 # #	* *** ***	# #	#	
(Ch. 571 (L. 125)	STHVPLTFCAGTKLELKR	SKAEPEDICIALCS Ō	DSCSCIDEILRI	XKAZNYEZGALDYEZ	9C 172
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	**	•		* * * * *	25.00
	ŌKĿĠŎSĿĸŗŗĸ			DIAMTÕTPLSLPVSL	9C472
		abcde 30	20	01	

FIG. 29

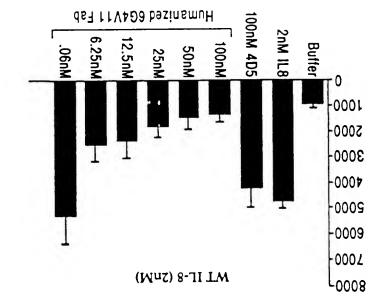
CMIHPSDSETRYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAARGIYFY-GTTYFDYWCQGT (SEG ID NC-50)

R3

IIImud

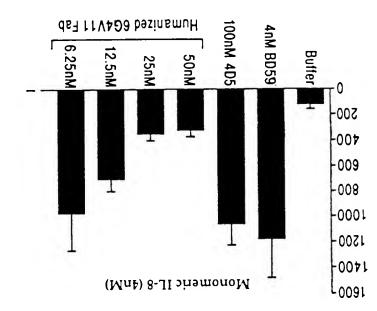


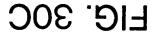
IC20~15nM



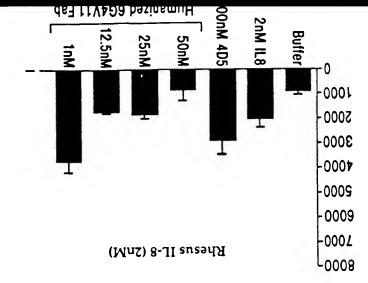
EIG. 30B

IC20~12uM





IC20~55uM



Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Light Chain

EC (SEQ ID NO: 51) ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG HVPLTFGQGTKVEIKRTVAAPSVFTFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGNTY LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQST

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Heavy Chain

MKKNIAFLLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH WVRQAPGKGLEWVGYIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY CARGDYRYNGDWFFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF VDKKVEPKSCDKTHT (SEG ID NO: 5'Z) PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK

Amino Acid Sequence of the peptide linker and M13 Phage Coat (gene-III)

GLANGNGATGDFAGSSNSQMAQVGDGDNSPLMNNFRQYLPSLPQSVECRPFVFSAGKPY SGGGSGSGDFDYEKMANANKGAMTENADENALQSDAKGKLDSVATDYGAAIDGFIGDVS EFSIDCDKINLFRGVFAFLLYVATFMYVFSTFANILRNKES (5E4 10 No: 53)

FIG. 31A

- 481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAC CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG 138 V C L L N N F Y P R E A K V Q W K V D N

- TADTTTADO DADOUTOTO DOCUMENTO TOTTGGGAD CONTROLLA INC TAGAGATOO DE CONTROLLA DE CON
- 181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC AATGTGACCA TAGTGATTTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG S L H W Y Q Q K P G K A P K L L L Y K V S

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Light Chain

ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG HVPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQST MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGNTY EC (SEQ ID NO: 51)

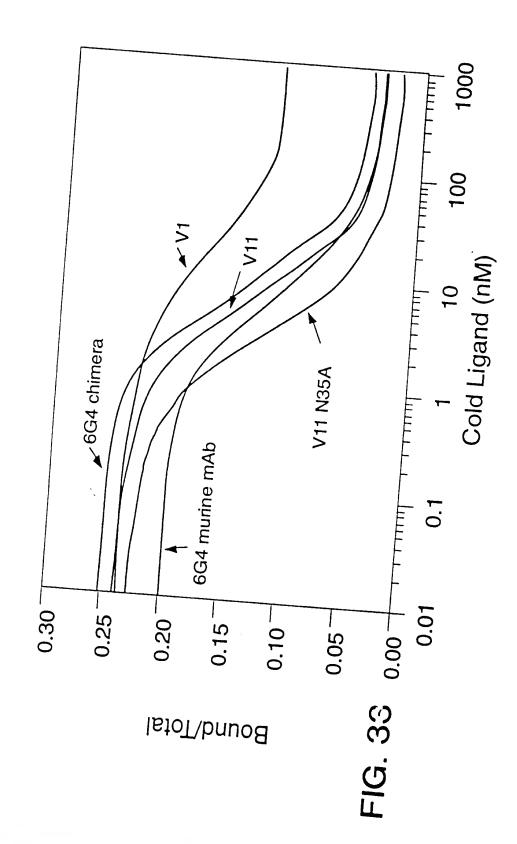
Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Heavy Chain

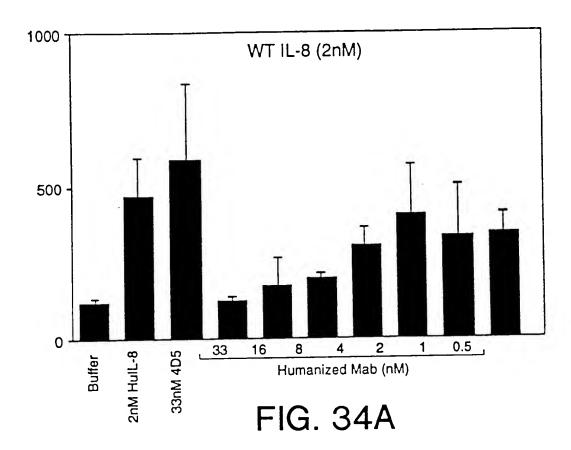
MKKNIAFLLASMFVFSIATNAYAEVQLVESGGGLVQPGGSLRLSCAASGYSFSSHYMH VDKKVEPKSCDKTHT (SEQ 10 NO: 55) CARGDYRYNGDWFFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF ${\sf WVKQAPGKGLEWVGYIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY}$ PEPVTVSWNSGALTSGYHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK

FIG. 31C



F16. 32





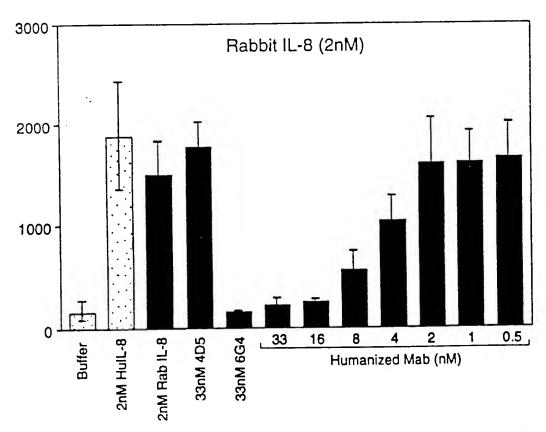
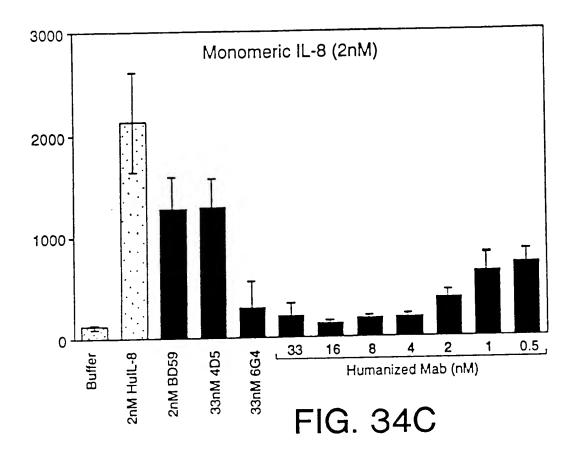
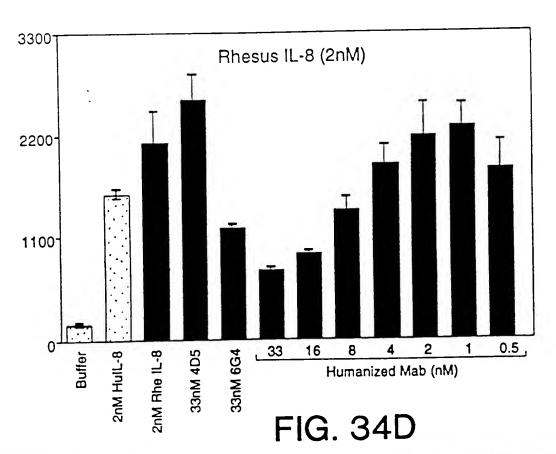


FIG. 34B





Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Light Chain

MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIG**A**TY LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQST HVPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG EC (SEQ ID NO: 56) anti-IL-8 6G4.2.5V11N35A Heavy Chain Amino Acid Sequence of the humanized

CARGDYRYNGDWFFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSSLGTQTYICNVNHKPSNTK WVRQAPGKGLEWVGYIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY MKKNIAFLLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH VDKKVEPKSCDKTHT (5EQ TO MO: 52 Amino Acid Sequence of the putative Pepsin Cleavage Site and GCN4 Leucine Zipper

CPPCPAPE<u>LL</u>GGRMKQLEDKVEELLSKNYHLENEVARLKKLVGER (5E4ID No:57)

FIG. 35

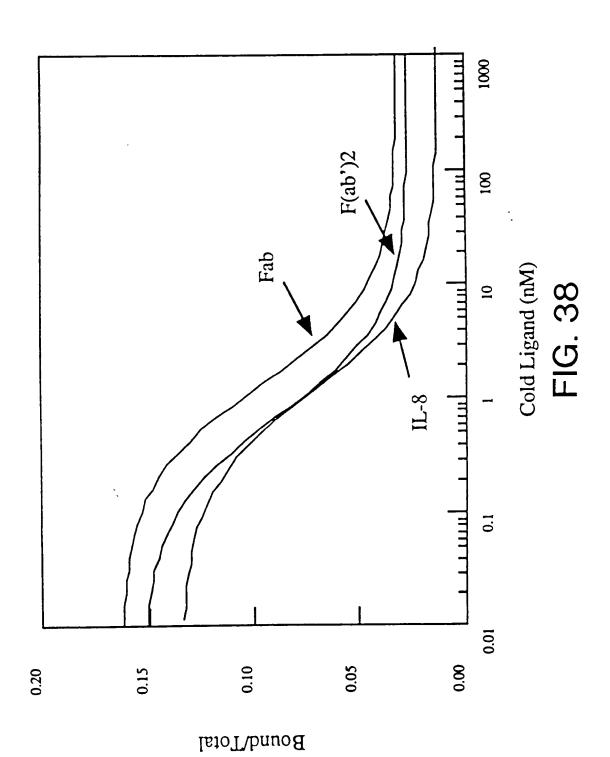
1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTCG TTTTTTCTAT TGCTACAAAC -23 M K K N I A F L L A S CAAAAAAAAAAAACATA ACCATGTTCAAAAAC
TACTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAAGATA ACGATGTTCG -23 M K K N I A F L L A S M F V F S I A TOTAGATACAAC 61 GCATACGCTG ATATCCAGAS
-23 M K K N I A F L L A S M F V F S I A T N CGTATGCGAC TATACCAGAT GACCCAGTCC CCCLOST CGTATGCACAGTCC CCCLOST CGTATGCACAGTCC CCCLOST CGTATGCACAGTCC CCCLOST CGTATGCACACT CGTATCCACACT CGTATGCACACT CGTATGCACAC
N I A F I AGATACAAGC AAAAAAC
OI GCATACOOM
CCMAmore TO CAGAT CAGATE
-3 A V TATAGGTCTA CTCCCTCC CCGAGCTCC TCTCCCT
61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGGGAT -3 A Y A D I Q M T Q S P S GGCTGAGGG ACAGGGGGAG ACACCCAGTC
CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA -3 A Y A D I Q M T Q S P S S L S A S V C C C C C C C C C C C C C C C C C C
1/CCO1 ==
18 R V T AGTGGACGTC CAGTTCAA AGCTTAGTAC ATCCTAGT
121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGCTACGTAT TCCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACGATGGTAT 18 R V T I T C R S S O S I TACCATATCC ACGATGGTAT
181 TTLCACRO
A Momos - Consort
38 L H W TAGTTGTCTT TGCTCCTTT
W Y Q Q K P C CAAGGCTTTG ATCAGTTTA CAAAGTATCC
241 AATCCAMMON
TTO COTA TO CO
241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA S N R F S G V P S R F S G S G S G T D F T GACTGGTAGT CCTGCA GCCAGAAGAC TTGGGAC GACTGGTAGT CCTGCA GCCAGAAGAC TTGGGAC GACTGGTAGT CCTGCA GCCAGAAGAC TTGGGAC TTGGACCATCA GCAGTCTGCA GCCAGAAGAC TTGGGAC GACTGGTAGT CCTGCA GCCAGAAGAC TTGGGAC TTGGACTAGATCTAGATCTGCA GCCAGAAGAC TTGGGAC TTGGACTAGATCTGCA GCCAGAAGAC TTGGACAC TTGGACTAGATCTGCA GCCAGAAGAC TTGGACACAC TTGGACTAGATCTGCA GCCAGAAGAC TTGGACACACACACACACACACACACACACACACACACAC
G V P S P S P S P S P S P S P S P S P S P
301 CTGACCAMO.
301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT 78 L T I S S L Q P E D F ATTACTGAA TAATGACAAG TETCTGTAACT
S L Q P E NAGCGTTGAA TAATCA CACAGAGTACT
361 CATGTCCCCC
GTACACCATTIGG ACACCACT
361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTCGCTGCA GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT 98 H V P L T F G Q G T K V E I K R T V A A GGTAGACAGA ACTION GCCATCTGAT CACCACCTCT AGTTTGCTTG ACACCGACGT 421 CCATCTGTCT TCATCTTCCC GCCATCTGAT CACCAC
F G O G T TTCCACCTCT AGTTTCCTTCA
\$21 CCamomomomomomomomomomomomomomomomomomom
Company - Calcarder Constant
118 P S V F I F P P S D E Q L K S G T A S V 120 CACACGGACG ACTTATION 130 CACACGGACG ACTTATION 131 CACACGGACG ACTTATION 132 CACACGGACG ACTTATION 132 CACACGGACG ACTTATION 133 CACACGGACG ACTTATION 133 CACACGGACG ACTTATION 134 CACACGGACG ACTTATION 135 CACACGGACG ACTTATION 135 CACACGGACG ACTTATION 136 CACACGGACG ACTTATION 137 CACACGGACG ACTTATION 138 CACACGGACG ACTTATION 138 CACACGGACG ACTTATION 139 CACACGGACG ACTTATION 130 CACACGGACGACGACGACGACGACGACGACGACGACGACG
F P P S D TTAGACT TTAGACCTTC ACCOUNT
481 GTGTGCCTCC
138 V C L L N N F Y P R E A K V Q W K V D N CGGGAGGTTA GCCCATTACTC CCAGGAGAGT GTCAGAGT CGGGAGGTTA GCCCATTACTC CCAGGAGAGT GTCAGAGT CACACGGAAAG TACAGTGGAA GGTGGATAAC CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC ATGTCACCTT CCACCTATTG CGGGAGGTTA GCCCATTGAGAGT GTCAGAGTAGTAGAGT CGGGAGGTTA GCCCATTGAGAGT GTCAGAGTAGTAGAGT CGGGAGGTTA GCCCATTGAGAGT GTCAGAGTAGTAGTAGAGT CGGGAGGTTA GCCCATTGAGAGT GTCAGAGTAGTAGTAGTAGTAGTAGTAGTAGTAGTAGTAGTAG
N N F Y P R F CICCGGTTTC ATGTCACCTT COLOR
541 GCCCTCCAATTG
CCCCCC COGGTAACTC CCCCCCC
541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC 158 A L Q S G N S Q E S V T TCCTGTCGTT CCTCTGTCGTT 158 C CACCTATTG 15
N S Q E S V M CAGTGTCTCG TCCTGTCGTT CCMCCACC
601 TACACCOTTO
178 Y S L S C TOCGACTCG TITTOCHER ACGAGAACA CANAGE
T L S K A TGCTCTTTGT CTTAC
661 GCCTCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
CGGACGCTTC AGTCCCTT AGGCCTGAGC TCGCCCCTT
661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGA C F V T H Q G L S S P V T K S F N R G 661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA 662 GCTGCGATCT CAACAGGGGA GTTGTCCCCT 663 GCTGCTTAAG CTGATCCTCT ACGCCGGACG CATCCTCA 664 GCTTCACAATTC GACTACCTCT ACGCCGGACG CATCCTCA
G L S S D TOTAL CANCAGGGGA
121 GAGTGTTAAG CTGATCCTCT
CTCACAATTC GACTAGGACA TOGGGGACG CATCGTGGG
218 E C O (SECTIO NO: 56) TGCGGCCTGC GTAGCACCGG GATCATGCCTA ACTAGTCGTA (SECTION: 58)
FIG. 36
1 IG. 36
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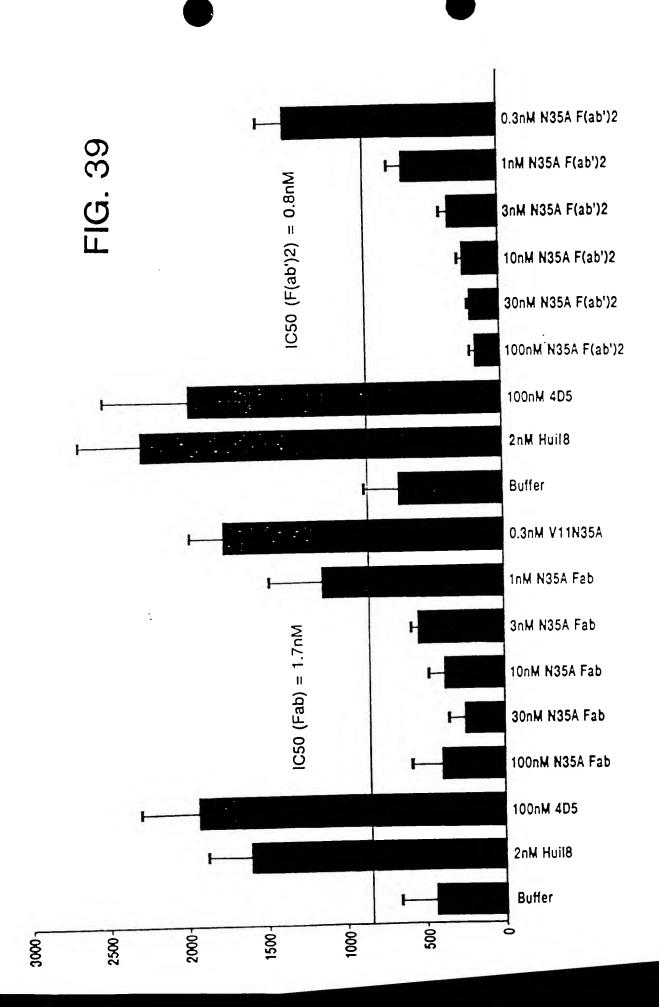
781 -1	TTT	AGC TCC	GT.	AT TA	CTAG. GATC	AGGI TCC <i>I</i>	TTG AAC	AGGT TCCA	GAT ACTA	AAAA	TAC	TTT	TTC	r '	TATA ATAT I	GCG"	raa	TCTT AGAA L	GAA	CGT
	AGA	TAC	AA"	GC	TTTT AAAA F	AAG	ATA	ACGA	ATG:	TTTG	CGC	CTAC	GCGA(C '	TCCA	AGT	_GA	TCAC	GIC	AGA
901	CCC	:CC	400	GG	TGGT ACCA V	CGT	CGG	TCCC		GAGT	GAC	3GC2	AAAC.	A	GGAC.	ACG.	100	AAGA		MIG
	AGO	A A	SAC	CT	GTCA CAGT H	GAT	ATA	CGT	GAC(CCAG	GC	AGT(CCGG	G	GCCC.	ATT	CCC	CCTC GGAC L	JC 1 1	ATGG FACC W
1021	CAR	יככי	דאת	TAT	TTGA AACT D	AGG.	AAG	GTT	ACC.	ACTT	TGI	ATG	CATA	T_{-}	TAGT	TTT	CAA	GII	رررر	JGCH
1081	AAC	TG	AAA	ATA	CTCG GAGC	GCT	GTT	GAG	GTT	AAAC TTTG N	TG'	TCG	TATG	G	ACGT	GAT CTA M	CTT.	GTC	CCT(GGA(L	CGCA
1141	GCT	GA CT	GG <i>F</i>	ACA TGT		CGT GCA	CTA GAT	AAT	GAC	ACGT	TC	TCC	CCTA	LΑ	TAGO	GAT	GTT	ACC.	ACT	GACC
1201	TT(TT: AAE	CG# GCT	ACG TGC	TCTC AGAC	GGG CCC	TCA AGT	AGG TCC	AAC TTG	CCTG GGAC	GT CA	CAC GTG	CGTC	T SA	CCTC	GGC	CTC GAG	CAC GTG	CAA	GGGC CCCG
1261	CC:	ATC	GG'	rct AGA	TCC(CCT GGGA	GGC 'GGC	ACC	CTC	CTCC GAGG	TT	CTC	CACC GTGC	ΞA	GACC	CCC	GTG	AGC TCG A		GGMC
1321	GG	OTO	, C.C.	TGG	TCA	AGG <i>A</i>	CTA CAT	CTT GAA	CCC	GCTI	'GG	CCA	CTGC	C	ACAC	CAC	CTT	GAG	ICC	CGCC GCGG A
1381	CT	GAC	CA	GCG	GCG'	TGC <i>I</i>	ACAC	CTT		CGGCT	GI CA	CCI AGG <i>I</i>	ACAC	GT CA	CCTO	CAGO	GACT CTGA	CTA GAT	CTC GAG	CCTC
1441	. AG	CAC	SCG	TGG	» ACT	CCG:	rgcc Acgo	CTC	CAC	GCAGO	TT :	rgg(CAC(CC GG	AGA(CCT/	ACAT TGTA	CTG	CAA GTT	CGTG
1501	S L AA	S TC	V ACA	AGC	CCA	V GCAJ TGC	P ACAC	S CAA GTT	S AGG! AGC!	S TCGA(AGCT(L A T	G AGA/ CTT	T AAGT' CTCA	Q TG AC	T AGC TCG	Y CCA GGT	I OTAA	C TTC AAC	N STGA SACT	V ACAAA GTTT
1561	N AC	H	K ACA	CAT	GCC	N CGC	T	K CCC	V CAG	D CACC GTGG	K A GA	K AAC'	V IGCT ACGA	E GG	P GCG CGC	K GCC CGG	S GCAI CGT	C GAA CTC	D AACA TTGT	K AGCTA ICGAT
228	3 T	H	. G1	` `		P	C	P	Α	'IG	Ε	L	L	G	; G	R	М	K	Q	L

1621 GAGGACAAGG TCGAAGAGCT ACTCTCCAAG AACTACCACC TAGAGAATGA AGTGGCAAGA CTCCTGTTCC AGCTTCTCGA TGAGAGGTTC TTGATGGTGG ATCTCTTACT TCACCGTTCT 248 E D K V E E L L S K N Y H L E N E V A R

1681 CTCAAAAAGC TTGTCGGGGA GCGCTAA (5EG IO NO: 59)
GAGTTTTCG AACAGCCCCT CGCGATT
268 L K K L V G E R O (5EG ID No: 60)

FIG. 37B





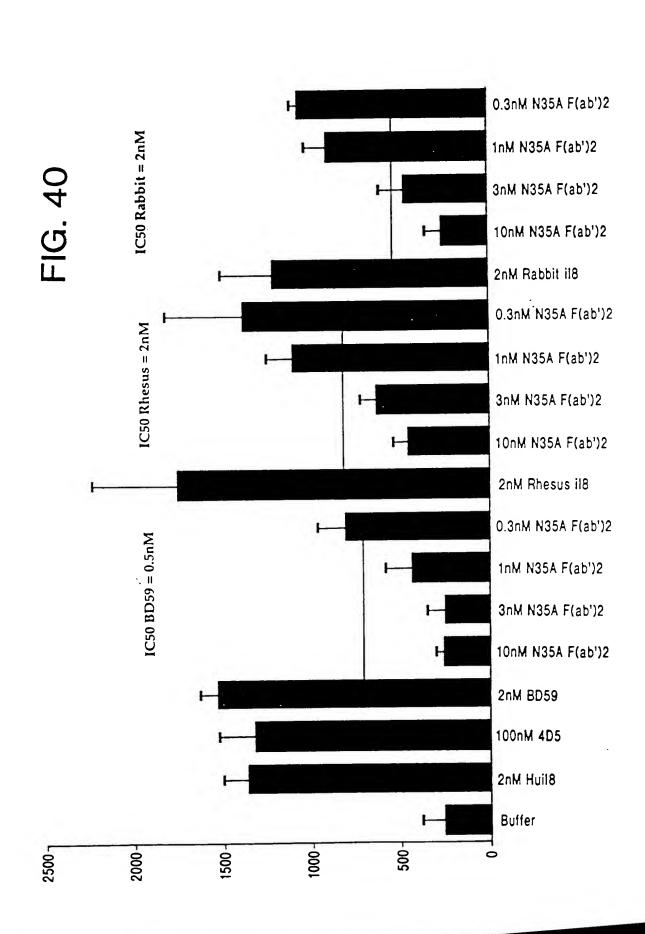


FIG. 41A

pleI mboII taqI earI/ksp632I mboII hinfI AAAAAGAAGA AGAGTCGAAT	sau3AI mbol/ndeII[dam-] dpnI[dam+] acil dpnII[dam-] nspBII bclI[dam-] mnlI ACCAACAGCG GTTGATTGAT CAGGTAGAGG	mnlI foki sfaNi TTGAAGCATC CTCGTCAGTA AACTTCGTAG GAGCAGTCAT	aluI sstI sacI hqiJII hqiJII hqiAI/aspHI ecl136II ecoRI bspl286 rmaI bsiHKAI maeI bmyI bfaI taqI maeIII apoI banII TTTGTAACTA GAATTCGAGC
aluI hindIII tru9I msel cac8I GTTGTTATTT AAGCTTGCC	acil nspbli ACCAACAGGG		tru9I mseI TTTTAATGTA
ddeI bsrDI TCATTGCTGA AGTAACGACT	hinPI hhal/cfol GCGCAAAATG CGCGTTTTAC	thal fuudHI bsoFI bbvI maeII fuudHI bstUI snaBI bsoFI bsh1236I bbvI hinPI bsaAI aluI hhaI/cfoI GAGCTGCTGC GCGATTACGT	1051 GTCGCTT TGTTTTATT
PflMI bsli TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC AGAGGTATGA AACCTATTCC TTATGTCTG TACTTTTAG	bspMI hinpI hhal/cfoI anul maeIII barDI aviII/fspI hindIII maeIII barDI GAACTGTGTG GCGAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGT TCGCAATATG CTTGACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCTTATAC	rsal hinpl hhal/cfol mnll cac81 haell csp61 sfanl bsml GGGCGCTGTA CGACGTAACG CCCGCGACAT GCTCCTAAGGACT GCTGCTATGC	haeIII/palI mcrI eagl/xmalII/eclXI eaeI cfrI b9iEI ahdI/eaml maeIII bsmAI
	bspMI hinPI hhal/cfoI mstI aviII/fspI hindIII TG CGCAGGTAGA AGCTTTGGA AC GCGTCCATCT TCGAAACCT	I I mnli cac8I 61 sfaNI CGAGGTAAAG CCCGATGCCA GCTCCATTTC GGGCTACGGT	ha mcr eag eac alui cfr pvuli bsi nspBII maeIII CTTTCAACA GCTGTCATAA AGTTGTCACG
ecori apoi 1 GAATTCAACT CTTAAGTTGA	hin hha msti avii 101 GAACTGTGTG C	rsal hinpi hhal/cfol mnli haeli csp61 201 GGCGCTGTA CGAGG	tru9I mBCI 101 AAAAGITAAT

!

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AGCCATGGGC CCCTAGGAGA GCTCCAACTC CACTAAAATA CTTTTTCTTA TAGCGTAAAG AAGAACGTAG ATACAAGCAA AAAAGATAAC GATGTTTGCG
M K K N I A F L L A S M F V F S I A T N A
                                                                                                                                                                                                                                                                                                                                                                                        401 TCGGTACCCG GGGATCCTCT CGAGGTTGAG GTGATTTTAT GAAAAAGAAT ATCGCATTTC TTCTTGCATC TATGTTCGTT TTTTCTATTG CTACAAACGC
                                                                                                                                                                                                                                                                                                                                                                                                                            a mutation was found that inactivated the mluI site. The penultimate nucleotide was changed fr G to T ^{\circ}
                                                                                                                                                                                                                                                                                                                                                                            mboli sfani
                                                                                                                                                                                                                                                                                                                                                               hphI
                                                                                                                                                                                                                                                                                                                                                                              alwi[dam-] muli muli
                                                                                                                                                                                                                                                 mbol/ndeII[dam-]
                                                                                                                                                                                                                                                                                   nlaIV paeR7I
                                                                                                                                                                                                                             sau3AI taqI
                                                                                                                                                                                                                                                                                                     kpnI cauII dpnII[dam-]
                                                                                                                                                                                                                                                                  dpnI[dam+]
                                                                                                                                                                                                                                                                                                                         bstYI/xhoII
                                                                                                                                                                                                                                                                                                                                             bani bsaJi alwi[dam-]
                                                                                                                                                                                                                                                                                                                                                               bamHI avaI
                                                                                                                                                                                        xhoI
                                                                                                                                                                                                          mnlI
                                                                                            xmaI/pspAI
                                                      hpall
SCLFI
                                                                         dsav
                                                                                                                                                                                        cauli
                                    Idem
                                                                                                                                 SCIFI
                                                                                                                                                                                                            bsaJI
                  ncil
                                                                                                               gma I
                                                                                                                                                   nciI
                                                                                                                                                                     dsaV
                                                                                                                                                                                                                              avaI
                                                                                                                                                                                                                                                                                                                                                                 asp718
                                                                                                                                                                                                                                                                                                                                                                                   acc651
                                                                                                                                                                                                                                                                    csp6I
                                                                                                                                                                                                                                                                                     nlaIV
                                                                                                                                                                                                                                                                                                                            hqici
                                                                                                                                                                                                                                                   rsaI
```

INTECCACTA INGGICTACT GGGICAGGGG CICGAGGGAC AGGCGGAGAC ACCCGCTAIC CCAGIGGIAG IGGACGICCA GIICAGIIIC GAAICAIGIA 01 ATACGCTGAT ATCCAGATGA CCCAGTCCCC GAGCTCCCTG TCCGCCTCTG TGGCCGATAG GGTCACCATC ACCTGCAGGT CAAGTCAAAG CTTAGTACAT bstEII hphi bsgI FIG. 41B

SSL

0 S P

TWOI

TCRS

ddel nlaili

sse8387I

bspMI

maelll

molI acil

bsrI avaI aluI tth1111/aspI banII

ecoRV

bmyI

DSmFI

pstI scfI

bspMI

hqiAI/aspHI

hgiJII

saci

ec1136II **bsp1286 bsinkai**

hindIII csp6I aluī

601 GGIATAGGIG CIACGIAITI ACACIGGIAI CAACAGAAAC CAGGAAAAGC ICCGAAACIA CIGAITIACA AAGIAICCAA ICGAITCICI GGAGICCCII CCATATCCAC GAIGCATAAA IGIGACCAIA GIIGICIIIG GICCIIIICG AGCTIIGAI GACTAAAIGI ITCATAGGII AGCIAAGAGA CCICAGGGAA bpmI/gsuI[dcm-] **DsmFI** clal/bsp106 bspDI[dam-] R F S tfir hinfi S > LIYK P K L aluI ∠ ∀ ∪ apy1[dcm+] ecoRII bstNI SCIFI dsaV mvaI O O K H H bsrI TYL

32 G I G A

G V P

hinfI

pleI

scal plail csp6I rsaI mbolI bpuAI bbsI fnu4HI bsoFI bbvI scfI pstI bsdI alwI[dam-] bsmFI mbol/ndell[dam-] dpnII[dam-] dpnI[dam+] bstYI/xhoII alwI[dam-] hpaII ball Idem DsaWI sau3AI nlaIV bamHI

701 CTCGCTTCTC TGGATCCGGT TCTGGGACGG ATTTCACTCT GACCATCAGC AGTCTGCAGC CAGAAGACTT CGCAACTTAT TACTGTTCAC AGAGTACTCA 1 TGTCCCGCTC ACGITTGGAC AGGGTACCAA GGTGGAGATC AAACGAACTG TGGCTGCACC ATCTGTCTTC ATCTTCCCGC CATCTGATGA GCAGTTGAAA ACAGGGGAG ICCANACCIG ICCCAIGGII CCACCICIAG IIIGCIIGAC ACCGACGIGG IAGACAGAAG IAGAAGGGCG GIAGACIACI CGICAACIII GAGCGAAGAG ACCTAGGCCA AGACCCTGCC TAAAGTGAGA CTGGTAGTCG TCAGACGTCG GTCTTCTGAA GCGTTGAATA ATGACAAGTG TCTCATGAGT SDE လ လ I F P P acil ATX Iloqu MbolI E D F Ppual ppsI SVF SLOP K R T V A A P fnu4HI **bsoFI** bbvI mbol/ndell[dam-] TIS dpnII[dam-] dpnI[dam+] sau3AI F T L VEI beaJI SGTD styI asp718 acc651 csp6I rsal nlaIV hgici kpnI banI T F G D e S maell barbi V P L acil **DamFI** R F

FIG. 41C

maeIII apyI[dcm+] bstNI bsaJI 101 TCTGGAACTG CTTCTGTTGT GTGCCTGCTG AATAACTTCT ATCCCAGAGA GGCCAAAGTA CAGTGGAAGG TGGATAACGC CCTCCAATCG GGTAACTCCC AGACCTIGAC GAAGACAACA CACGGACGAC TIAITGAAGA TAGGGTCTCT CCGGTTTCAT GICACCTTCC ACCIAITGCG GGAGGITAGC CCAITGAGG GNSO LOS ball mnlI N > X X csp6I rsal haeIII/palI PREAKV haeI mnlI N Fi asp700 XmnI ر 1 cac8I > × asp700 Iomx

ecoRII

dsav

BCLFI

mvaI

fnu4HI

ddeI

celII/espI bsoFI acci cac8i hqaI ddeI Indd Ilnm scfI

blpI/bpull02I

01 AGGAGAGTGT CACAGAGCAG GACAGCAAGG ACAGCACCTA CAGCCTCAGC AGCACCCTGA CGCTGAGCAA AGCAGACTAC GAGAAACACA AAGTCTACGC TCCICTCACA GIGICICGIC CIGICGIICC IGICGIGGAI GICGGAGICG ICGIGGGACI GCGACICGII ICGICIGAIG CICIIIGIGI IICAGAIGCG VYA EKHK A D Y L S R STLIT SLS T X Ŋ Ω maeIII

hqiAI/aspHI ec1136II **bsp1286** cac8I **DS1HKAI** hgiJII aluI haeIII/palI Bau96I banII BStI BacI DmyI asul ddel

mael bfaI sau96I hgaI mbol/ndeIl[dam-] aluI dpnI[dam+] sau3AI

I mu

mnlI

haeIII/palI asuI hpall sfaNI dpnII[dam-] mspI alwI[dam-] tru9I msel

CIGCGAAGIC ACCCAICAGG GCCIGAGCIC GCCCGICACA AAGAGCIICA ACAGGGGAGA GIGTIAAGCI GAICCICIAC GCCGGACGCA ICGIGGCCCI GACGCTTCAG TGGGTAGTCC CGGACTCGAG CGGCAGTGT TTCTCGAAGT TGTCCCTCT CACAATTCGA CTAGGAGATG CGGCCTGCGT AGCACCGGGA \mathbf{c} \mathbf{c}

aluI

maelll

eco01091/drall

alwNI[dcm-]

maelil

FIG. 41[

```
1301 CTACAAACGC GTACGCTGAG GTTCAGCTAG TGCAGTCTGG CGGTGGCCTG GTGCAGCCAG GGGGCTCACT CCGTTTGTCC TGTGCAGCTT CTGGCTACTC
                                                                                                                                                                                                                                                                                                           GATGITIGCS CATGCGACIC CAAGICGAIC ACGICAGACC GCCACCGGAC CACGICGGIC CCCCGAGIGA GGCAAACAGG ACACGICGAA GACCGAIGAG
                                                          TCATGCGTTG ATCAGCATTT TTCCCATAGA TCTCCAACTC CACTAAAATA CTTTTCTTA TAGCGTAAAG AAGAACGTAG ATACAAGCAA AAAAGATAAC
                                           1201 AGIÁCGCAAC TAGICGIAAA AAGGGIAICT AGAGGIIGAG GIGAITITAT GAAAAAGAAT AICGCAITIC TICTIGCAIC TAIGIICGII TITICIATIG
                                                                                                                                                                                                                                    alwNI[dcm-]
                                                                                                                                                                                                                                                   fnu4HI
                                                                                                                                                                                                                                                                 bsoFI
                                                                                                                                                                                                                                                                                  bbvI
                                                                                                                                                                                                                       aluI
                                                                               L A S
                                   mbolI sfaNI
                                                                                IAFL
                                                                                                                                                                                                                                                                                                                                G S L
                                                                                                                                                                                                                                         bsp1286
                                                                                                                                                                                                                                                                                     banll
                                                                                                                                                                                                                                                    apy1[dcm+] bsaJI bmyI
                                                                                                                                                                                                                                                                    haeIII/pall apy1[dcm+]
                                                                                                                                                                                                                         dsav bstNI hgiJII
                                                                                                                                              ecoRII
                                                                                                                                                                                                                                                                                                                                V Q P G
                                                                                                                scrFI
                                                                                                                                                              dsaV
                                                                                                                                mvaI
                                                                                   N
N
                                                                                                                                                                                           fnu4HI
                                                                                                                                                                                                                                        bstNI bsoFI
                                                                                                                                                                                                                                                                                       bbvI
                                                                                                                                                                                                           ecoRII
                                                                                                                                                                              SCLFI
                                                                                                                                                                                               mvaI
                                                                                                                                                                                                                                                                                                                                     n
L
                                                                                                                                                                                                                                                                                       acil hael
                                                                                                                                                                                                                                                                                                                                       v
                            hphI
                                        xbal mull mull
                                                                                                                                                                                                                                                                                                                                       o
s
o
            mael
                            bfaI
rmaI
                                                                                                                                                                                                                                                                                                                                        A O L V
                                                                                                                                                                                                                                                                             bfaI
                                                                                                                                                                                                                                                rmaI
                                                                                                                                                                                                                                                               maeI
                                                                                                                                                                                                                                                                              mluI cap6I mnlI
                                                                                                                                                                                                                                                                                                                                           Y A E
                                                                                                                                                                                                    DsiWI/spli
                                                                                                                                                                                                                                 funDII/mvnI
                                                                                                                                                                                                                                                                bsh1236I
                                                                                                                                                                                     rsaI
                mael
                                bfaI
    rmaI
                                                                                                                                                                                                                                                   batuI
                                                                                                                                                                                                                                                                                                                                            H
N
                                  rsaI
```

ecoRII SCLFI mvaI xmaI/pspAI cauli hpaII Idsm dsaV caull ball SCIFI ncil dsaV bslI smaI ncil

SCIFI

FIG. 41E

		/palI	
maell snaBl hphl bsaAl ATGGTGAAAC TACGTATAAT TACCACTTTG ATGCATATTA	GCCGTCTATT CGGCAGATAA A V Y Y	sau96I haeIII/palI sau96I nlalV hgiJII bsp1286 bsp120I bmyI I bap1Z apaI apaI styI asuI mnlI bsaJI rCGCCTCCA CCAAGGCCC AGCCGAGGT GGTTCCCGGG S A S T K G P 255chim2.fab2	
	cac81 mn11 cac81 dde1 drd1 GCCTGCGTGC TGAGGACACT CGGACGCACG ACTCCTGTGA L R A E D T	TC TC S S S S S S S S S S S S S S S S S	
bsli sau3Al mbol/ndell[dam-] dpnl[dam-] alwl[dam-] ATATT GATCCTTCCA TATAA CTAGGAAGGT	cac81 cac81 cA GCTGCTGC GT CGGACGCACC	maeIII bstEII scrFI mval mval ecoRII bsaJI dsav bseRI bstNI esp31 bsaJI hphI bsmBI mnlI b nlaIV apyI[dcm+] bsmAI haeIII/pal G GAACCCTGGT CACCGTCTC TCGGCGTCG C G T L V T V S S A S T seq right is from p6G425chim2.fab2	
mbol, dpn[] TGGATATAT	CAGATGAA GTCTACTT Q M N	ma bst scrFI mvaI ccoRII dsaV bstNI bsaJI h nlaIV apyI(d G GAACCCTGGT C T L V seq right	=
pleI bsaJI dsaV aval bstNI bsaJI bslI bsaJI bslI bsaJI bslI avaII nlaIV sau96I paeR7I asuI haeIII/palI asuI avaI haeIII/palI asuI avaI eco01091/draII dpnII[avaI eco1091/draII asuI avaI evo1091/draII asuI avaI eco1091/draII asuI avaI eco1091/draII asuI avaI eco1091/draII avaI eco1091/draII asuI avaI eco1091/draII avaI eco1091/draII asuI avaI eco1091/draII asuI	bs AGCATAC TCGTATC	maeIII pari maeIII pari abaII/bsaiI pari bati bati bati bati abaII/bsaiI bati bati bati bati bati apai apai apai apai bati bati bati bati bati bati bati apai apai apai bati bati bati apai apai apai bati bati bati bati apai apai bati bati apai apai apai apai bati apai a	- - - -
bsaJI dsaV aval bstNI bsaJI bslI sau96I apyl[dcm+ nlaIV sau96I haeIII/palI asuI asuI ecol091/draII haeIII/palI AGGCCCG GGTAAGGGCC TGGAAT TCCGGGGC CCATTCCCGG ACCTTA	vnI CT CCAAAAAC GA GGTTTTTG S K N	maell hinll/s ahall/maell hphl bsrl mboll aatll c GTGACTGGTT CTTCGACGTC CACTGACGTC GACTGCTG G D W F F D V	-
bsad aval bsaJI is sau96I nlaIV haeIII/ asuI eco0109I ig TCAGGCCCG	thal fnuDII/m bstUI bshl236I nruI CT CGCGACAA SA GCGCTGTT	maelii hphi bsri TG GTGACTG AC CACTGACG	
sau96I avaII asuI nlaIV bsrI cc ACTGGGTCCG	Palí T CACTITATC NA GTGANAIAC F I S	AT CGCTACAA'	
I fI aeIII T CACTATATGC A GTGATATACG	haeIII/palí sau96í asul CA AGGCCGTTT CA GT TCCCGCAAA GT K G R F T	mnli NG AGGGATT/ FC TCCCTAA:	
	01 CAAAAGITC GTTITCAAG	m 1 ACTGTGCAAG TGACACGTTC 6 C A R	
1401	501		

hphi mspi hpali cfr101/bsrFi bsawi tth1111/aspi bsli agel maeIII rccccGAACC GGTGACGGTG
Dear Dear
nlaIV hgiCI banI scrFI mvaI ecoRII dsaV hgiAI/aspHI dbaUAI apyI[dcm+] mnlI bsiHKAI bbsI baaJI mnlI bmyI mnlI ATCGGTCTTC CCCTGGCAC CCTCTCTCTTGCAAG GGGACCGTG S V F P L A P S S K S T S

SCIFI

mvaI

					•	1	bsofi maeili mbli		bsu36I/mstII/sauI mnlI bbvI bstEII bmyI bpmI/gsuI[dcm-]	TCGTGGAACT CAGGCGCCT GACCAGCGGC GTGCACACCT TCCCGGCTGT CCTACAGTCC TCAGGACTCT ACTCCCTCAG CAGGGTGGTG ACCGTGCCT	ACCACCTTGA GICCGCGGGA CIGGICGCCG CACGIGIGGA AGGGCCGACA GGAIGICAGG AGICCIGAGA IGAGGGAGIC GICGCACCAC IGGCACGGA	PAV LQS SGLY SLS SVV TVP S
						ddel	muli plei	eco811 hinfI	scfI bsu36I/mstII/s	ST CCTACAGTCC TCAGGACTCT	CA GGATGTCAGG AGTCCTGAGA	V LQSSGLY
		'aspHI	9.	Iqem Iv	hpall	SCIFI	ncil	apaLI/snol dsaV	[/snol caull	ACCT TCCCGGCT	STGGA AGGGCCGAC	TFPA
	u	hg1AI/aspHI	bsp1286	DSTHKAI	[cac8I	fnu4HI	bsofi bmyl	acii apali/	ddel ahall/bsaHl nspBll alw441/snol caull	SACCAGCGC GTGCAC	CTGGTCGCCG CACGTG	T S G V H
hinpi	hhaI/cfoI	nlaIV	narI	kası	hinlI/acyI	hq1CI	haell	banI	ddel ahall/bsal	TCGTGGAACT CAGGCGCCCT (AGCACCTTGA GTCCGCGGGA	SWNS GALTSGVHTF

CCAGCAGCTT GGGCACCCAG ACCTACATCT GCAACGTGAA TCACAAGCCC AGCAACACCA AGGTGGACAA GAAAGTTGAG CCCAAATCTT GTGACAAAAC GGTCGTCGAA CCCGTGGGTG TGGATGTAGA CGTTGCACTT AGTGTTCGG TCGTTGTGGT TCCAGCTGTT CTTTCAACTC GGGTTAGAA CACTGTTTG S S L G T Q T Y I C N V N H K P S N T K V D K K V E P K S C D K T maeIII bsp1286 hgiJII styl hincll/hindll bmyl bsayl acci banll taqi sall bsaJI accI hinfI tfiI maell **bsp1286** nlaIV hgici banI bmyI aluI fnu4HI baoFI ppvI bstXI

FIG. 41G

maeI bfaI rmaI 2001 TCACACATGC CCGCCGTGCC CAGCACCAGA ACTGCTGGC GGCCGCATGA AACAGCTAGA GGACAAGGTC GAAGAGCTAC TCTCCAAGAA CTACCACCTA AGTGTGTACG GGCGGCACGG GTCGTGGTGTT TGTCGATCT TTGTCGATCT CCTGTTCCAG CTTCTCGATG AGAGGTTCTT GATGGTGGAT Y H L S earI/ksp632I O L E D K V E E L L taqI aluI Iloqm sapI tth1111/aspI aluI mnlI bfaI rmaI maeI eagl/xmaIII/eclXI nlaIII PPCPAPELLGGRMK function between antibody and leucine zipper acil acil bsoFI bsiEI fnu4HI mcrI cfrI eael notI **bsp1286** nspHI acil bmyl nlaIII Idsu

hacIII/palI

fnu4III

bsoFI

ncil	Idsm	hpall	dsaV	cauli	acil	fnu4HI	bsoFI	GICGGGGAGC GCTAAGCAIG CGACGGCCCI AGAGICCCIA AGGCICGGII GCGGCGGGG GIIIIITAII CAGCCCICG CGAIICGIAC GCIGCCGGGA ICICAGGGAI IGCGAGCCAA CGGCGGCCCG CAAAAAIAA	
		rmaI	maeI	bfaI bsmFI	sau96I pleI	haeIII/palI	asuI hinfI	ACGCCCT AGAGICCCIA ACO IGCCGGGA ICICAGGGAI IGO	: 60)
Idqs	ddel nlaill	cell1/espI	blpI/bpull02I	hinPI nspI	hhaI/cfoI	haell nspHI	eco47III cac8I	GGGGAGC GCTAAGCATG CGA	V G E R O (56419 10: 60)
						aluI	hindili		:
						pleI	hinfi	2101 GAGAATGAAG TGGCAAGACT CAAAAAGCTT	262 E N E V A R L K K L

SCIFI ncil

FIG. 41H

2201 GITAACICAT GITIGACAGC ITAICAICGA TAAGCITTAA IGCGGIAGIT IAICACAGIT AAAITGCIAA CGCAGICAGG CACCGIGIAI GAAAICIAAC CAATIGAGIA CAAACIGICG AATAGIAGCI AIICGAAAII ACGCCAICAA AIAGIGICAA ITIAACGAII GCGICAGICC GIGGCACAIA CIITAGAIIG

bspDI[dam-] msel acil

aluI

hincII/hindII hpaI nlaIII

tru91 mseI

clal/bsp106 tru91 taqI hindIII

hgici nlaIV

> tru9I msel

banI

SOURTI MALE STATE STATE SOURTI MALE SOURTI SASI MEDI ACTOR SOURTI SASI MEDI MEDI MALE SOURTI MALE SOURTI SASI MEDI MALE SOURTI MALE SOURTI SASI MEDI MALE SOURTI MALE SOURTING SOURTICGAR SOURTING MALE SOURTING SOURTING SOURTING MALE SOURTING SOURTING SOURTING SOURTING MALE SOURTING MALE SOURTING SOURTING MALE SOURTING SOURTING MALE SOURTING SOURTING MALE SOURTING MALE SOURTING SOURTING MALE SOURTING MALE SOURTING MALE SOURTING SOURTING MALE SOURTING SOURTING MALE SOURTING MALE SOURTING MALE SOURTING MALE SOURTING SOURTING MALE MALE SOURTING MALE MALE SOURTING MALE MALE SOURTING MALE MALE SOURTING MALE MALE SOURTING MALE MALE MALE MALE SOURTING MALE MAL	
haell/pall sau961 scrit ncil csp61 hpall csp61 hpall msp1 dsaV bsl1 hpall caull actil cfr101/bsrF1 asul actil cAACCAA TACGGCCATG ACGCCCGGA GAACGCCCTA TAGCAGG GAACCAB hpall hhal/cfol bsp1286 actil mst1 bsl1 bsl1 bslHKAI mcrI avi11/fsp1 bmyI bsiEI cAATTTC TATGCGCAC GCAAGAGCCT CGTGACGGAA	
haeIII/palI sau961 scrFI ncil csp61 hpalI msp1 dsav bsl1 cfr101/bsrFI asu1 acil cTTGGTT ATGCGGTAC TGCGGGCT CTTGCGGAT A GAACCAA TACGCCATG ACGCCCGGA GAACGCCCTA T hinPI hgiAI/aspHI hhal/cfoI bsp1286 mst1 bsl1 bslHKAI mcrI aviII/fsp1 bmyl bsiE	
haeIII/pall sau961 scrfl ncil rsal mspl mnli csp61 hpall mspl caull cfr101/bsrFl asul aci fr101/bsrFl asul aci cAACCAA TACGGCATG ACGGCCGGA GAACGG GAACCAA TACGGCATG ACGGCCGGA GAACGG GAACCAA TACGGCATG ACGCCCGGA GAACGC GAACTTC TATGCGCACC CGTCTCGGA GCACTG GTTAAAAG ATACGCGTGG GCAAGAGCCT CGTGA	
haeIII sau961 ncil rsal mspl mnli csp61 hpall mspl dsaV bsl] hpall caull cfr101/bsrFl asuI cTTGGTT ATGCGGTAC TGCGGGCT GAACCAA TACGCCATG ACGCCCGGA hinpl hal/cfol bsj mstl bsll bm cAATTC TATGCGCACC CGTACCGGA GTTAAAAG ATACGCGTGG GCAAGAGCCT	
sau961 sau961 rsal ncil csp61 hp msp1 ds hpall ca cfr101/bsrFI CTTGGTT ATGCGGTAC TGC GAACCAA TACGCCATG ACGG mst1 bs11 avi11/fsp1 CAATTTC TATGCGCAC GCT	
rsal ms csp mspl hpall cfr101/ CTTGGTT ATGCCGGTA GAACCAA TACGCCCAI hhal/cmstl b avill/i	
CTTGGTT ATGGAACCAA TAGGAATTTC TAGGTTAAAG ATGGTTAAAG ATGGTTAAAAG ATGGTTAAAAAG ATGGTTAAAAAAAA	
CTTG	
T AGGC A TCCC A TCCC A TCCC A TCCC C ATGC	
CCGTA 7	
T Scfi Scfort GACAT C. C.f.OI	
scrFI mval ecORII dsav hlaIV bstNI hgiCI bsaJI banI maeIII fokI scfI GGCACCGTC ACCTGGATG CTGT CCGTGGCAG TGGACCTAC GACA I maeI hhaI/cfoI rmaI maeI nheI fnu4HI haeII bbvI bfaI cac8I cac8I cac8I cac8I cac8I cac8I cac8I cac8I	
scrFI mvaI ecoRII dsav dsav tv bstNI st bsaJI hph apyl [c I maeIII fo) ACCGTC ACCTGGA TGGCAG TGGGACCT TGGCAG TGGGACCT TGGCAG TGGGACCT TMaEI nheI nheI bbvI bfaI cac8I cac8I GCGTGC TGCTAGCC	
nlaIV hgiCI banl r GGCACCG CCGTGGC	
nlaIV mnli hgiCi bsaJi oki bani ATCCT CGGCAC TAGGA GCCGTG TAGGA GCCGTG GTCAC TATGGC CAGTG ATACCG	
PI I/cfol fok CTCA TCGTCAT SAGT AGCAGTA BfaNI bBrI GCAT CGCCAGT	
mnli hinPi bsaJi hhal/cfoi foki GCGCTCA TCGTCATCCT CGCGAGT AGCAGTAGGA (CGCGAGT AGCAGTAGGA (CGCAGTCAC);	
h: hI TTACK TTACK TGGA	

CCGCCCCCA GICCIGCICG CIICGCIACI IGGAGCCACI AICGACIACG CGAICAIGG GACCACACC GICCIGIGGA ICCICIAGG CGGACGCAIC GGCGGCGGGI CAGGACGAGC GAAGCGAIGA ACCICGGIGA IAGCIGAIGC GCIAGIACCG CIGGIGIGG CAGGACACCI AGGAGAIGCG GCCIGCGIAG hpall sfani hgaI Idsm dphl[[dam-] alw[[dam-] bstYI/xhoII dpnI[dam+] alwI[dam-] nlaIV bamHI bslI mbol/ndeII[dam-] dpnII[dam-] dpnI[dam+] bstUI nlaIII funDII/mvnI bsh1236I taqI nlaIV cac8I acil berI fnu4HI bsoFI acii

mbol/ndell[dam-]

sau3AI

sau3AI

FIG. 41I

										hgiJii haeli	bsp1286 eco4/III	bmyl bsphil hnal/croi	banII nlalil	TCGGG CTCATGAGCG AGCCC GAGTACTCGC
				!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!	III)	0301286	Iwa	banII	sau3AI cac8I	mbol/ndell[dam-]	dpnI[dam+]	dpnII[dam-]	mpoll[dam-]	C GATGGGGAAG ATCGGGCTCG CCACT C CTAUCCCTTC TAGCCCGAGC GGTGF
			hinPI	hhaI/cfoI	nlaIV	narI	kasī 💛	hinl1/acy1	hgiCI	haeII	banI	ahaII/DsallI	acii cac8i hphi	601 GIGGCCGGCA ICACCGGCGC CACAGGIGCG GIIGCIGGCG CCIAIAIACGC CGACAICACC GAIGGGGAAG AICGGGCICG CCACIICGGG CICAIGAGCG CACCGGCCGI AGIGGCCGCG GIGICCACGC CAACGACCGC GGAIAIAGCG GCIGIAGIGG CIACCCCIIC IAGCCCGAGC GGIGAAGCCC GAGIACICGC
hinpi	hhaI/cfoI	nlaIV	narī	kasI	hinlI/acyI	mspI hgiCI	н	nael mspl	I/bsrF	cac8I sqrAI	haeIII/pall hpall	eael hphl ahall/bsaHl	cfrl sfaNi cfr101/bsrFI	501 GTGGCGGCA TCACCGGCGC CACAGGT CACCGGCCGT AGTGGCCGCG GTGTCCA

haeIII/palI 1 CTTGTTTCG CGTGGGTATG GTGGCAGGCC CCGTGGCCGG GGGACTGTTG GGCGCCATCT CCTTGCACGC ACCATTCCTT GCGGCGGCGG TGCTCAACGG GAACAAAGCC GCACCCATAC CACCGTCCGG GGCACCGGCC CCCTGACAAC CCGCGGTAGA GGAACGTGCG TGGTAAGGAA CGCCGCCCCC ACGAGTTGCC bsofi hgiAI/aspHI **bsp1286 DSIHKAI** bmyI bsll acil acil fnu4HI acil fnu4HI bsoFI cac8I ahaII/bsallI hhal/cfol hinl1/acy1 nlaIV hinPI hgiCI haeII DanI kasī narI **DSmFI** sau961 haeIII/pall caull hpaII asul bsaJl bsaJl dsaV ncil Idem eco01091/drall eael cac8I bslI cfrI haeIII/palI dsaI ball nlaIV

SCLFI

hpaII CCTCAACCIA CTACTGGGCT GCTICCIAAT GCAGGAGICG CATAAGGGAG AGCGICGICC GAIGCCCIIG AGAGCCTICA ACCCAGICAG CICCTICCGG GGAGTIGGAT GAIGACCCGA CGAAGGAITA CGICCICAGC GIATICCCIC ICGCAGCAGG CIACGGGAAC ICICGGAAGI IGGGICAGIC GAGGAAGGCC Idem bgaWI bsrI aluI bslI sfaNI hqaI hinfI pleI ecoNI bslI fnu4HI bsoFI bsrI bbvI Iled Ilum

FIG. 41J

```
2901 TGGGGGGG GCATGACTAT CGTCGCGGCA CTTATGACTG TCTTCTTTAT CATGCAACTC GTAGGACAGG TGCCGGCAGC GCTCTGGGTC ATTTTCGGCG
                                                                                              ACCCGCGCCC CGTACTGATA GCAGCGCGT GAATACTGAC AGAAGAAATA GTACGTTGAG CATCCTGTCC ACGGCCGTCG CGAGACCCAG TAAAAGCCGC
                                                                                                                                                                                                                                  3001 AGACCGCTT TCGCTGGAĞC GCGACGATGA TCGGCCTĞTC GCTTGCGGTA TTCGGAATCT TGCACGCCCT CGCTCAAGGC TTCGTCACTG GTCCGCCAC
                                                                                                                                                                                                                                                TCCTGGCGAA AGCGACCTCG CGCTGCTACT AGCCGGACAG CGAACGCCAT AAGCCTTAGA ACGTGCGGGA GCGAGTTCGG AAGCAGTGAC CAGGGCGGTG
                                                                                                                                                                                    sau96I
                                                                                                                                                                                                     nlaiv
                                                                                                                                                                                                                   avall
                                                      cac8I eco47III
            mspl hinpl
                                        cfr101/bsrFI
                           haeII
fou4HI
                                                                        bsoFI
                            naeI
                                                                                                                                                                                                                                 tfir
                                                                                                                                                                                                                             acil
                                                  Ilodm '
                                                                       IVndq
                                                                                                                                                                         haeIII/palI
                                                                                                                                                                                                    mbol/ndell[dam-]
                                                                                                                                                                                                                            bpmI/gsul[dcm-] dpnII[dam-]
                                                                                                                                                                                                                    dpnI[dam+]
                                                                                                                                                                                 bsh1236I sau3AI
                                                                 fnu4HI
                                                                                                                                                    fnuDII/mvaI
                                                                                                                                                                                                                hhaI/cfoI
                                                                                                                                                                       bstur
                                                                                                                                                                                                 hinpr
                           bstUI plaIII
           fnuDII/mvnI
                                                            bcgI
                                         bsh1236I
                                                                      hhaI/cfoI
                                                        hinpi
                                                                                                                                                                                acii
                                                                                                                                                                                             I96nes
                                                                                                                                                                                                             avaII
```

bsh1236I fokI haeIII/palI GTTIGCAANG CCGCTCTICG ICCGGTAATA GCGGCCGINC CGCCGGCTGC GCGACCCGAI GCAGAACGAC CGCAAGCGCT GCGCTCCGAC CTACCGGAAG 101 CAÀACGTTTC GGCGAGAAGC AGGCCATAT CGCCGGCATG GCGCCGACG CGCTGGGCTA CGTCTTGCTG GCGTTCGCGA CGCGAGGCTG GATGGCCTTC thal fnuDII/mvnI fnuDII/mvnI bstur bstur thaI hqaI fuuDII/mvnI hhaI/cfoI bsh1236I batul thaI acil hgal bsiEI fnu4HI cfrI bsoFI cfr101/bsrFI haeIII/pall hpaII cac8I psp14061 maell

eagI/xmaIII/eclXI

hinpI

eael

FIG. 41K

alwI[dam-] .G .C	
alw! [nlaiii CATG
bsmFI aluI GGGA CAGCTTC CCCT GTCGAAC	GGTTGG
bsmF] rcagggA	aspHI 6 1. nlaIII cATGGAACG
GGA CCA	hgiAI/aspHI bsp1286 bsiHKAI bmyI cac81 nlaII GCGAGC ACATGG
IAGATGA	mnll bsaJI h I b HI b I cac
bspMI scrFI mvaI ecoRII dsaV bstNI apyI[dcm+] rCCAGGCAGG	mn bs. acil fnu4HI bsoFI bg1I rttatGCGC
thai thai scrfi fundii/mvni mvai ecoRii ecoRii haei dsav sfaNi bsh1236i haeiii/pali bstNi bsh1236i nlaili apyi[dcm+] bsmFi alui aloki acii cac8i nlaili apyi[dcm+] bsmFi alui aloki cacGcTTGCT TCCAGGCAG TACATGAGGA CACCTTCAAG CATCAAGGA CACCTTCAAG CATCAAGTTC	fnu4HI bsoFI acil thai thai thai thai bstUl cac8I aaulAl bshl236I mboI/ndeII[dam-] mboI/ndeII[dam-] dpnI[dam+] dpnI[dam-] dpnI[dam-] dpnI[dam-] dpnI[dam-] dpnI[dam-] dpnI[dam-] cacGCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
thai fuuDII/mvnI bstUI hae II cac8I cciI cac8I cciCCTTGCA G	61 I sau3AI mbol/ndeII[dam-] nspBII maeIII aciI dpnI[dam+] cCGCTGATC GTCACG
	sau96I avall bsrl sau3AI asul mh mbol/ndeIl[dam-] dpnI[dam+] nspBII dpnI[dam-] acil dl GATCACTGG ACGGTG
fnu4HI bsoFI acil sfaN hpaII sfaNI fokI ccGGCGCC ATCGGCATC	s. bsri sau3Al a mbol/nde dpn1[dam dpn1[dam-] taq1[dam-]
fnu4HI bsoFI aciI mspI ms hpaII sfa TTCCGCCGC	AGCCTAAC TCGGATTC
fnu4HI bsoFI cac tfiI mspI mslI sfaNI hinfI binfI cac scorrate and stani fokI Andangaggg Anggccgcagg TagcccTACG	/mvnI 51 a-] CTCTTACC
mb tfii hinfi NTGA TTC	fnu4HI bsoFI acil thai thai fnuDII/mvnI bstUI cac8I maol/ndeII[dam-] dpnI[dam+] dpnI[dam+] GATGGTTGC GGCTCTT CTAGGAGGG CCGAGAA
CCCATTA	fnuo bsol acti thai thai fnub bstU cac@! sau3AI bshl mboi/ndeii[dpni[dam+] dpni[dam+] catcGCTCGC
3201	101

haeIII/pall fnu4HI sau961 scrFI scrFI thal ncil mspl fnuDII/mvnI mspl hpaII hpaII hpaII hpaII nael hglCI bstUI bstU36 nlaIV asul taqI cac81 banI ccrCCCCCC TTCCTCCCC GCCATCGAC CCGCACCTCG GGAGGGCCC AACCACCC CACGTACCTC GCCCGTGG ACTTCGCC CCCTGGACT	
haeIII/pall sau961 scrFI thaI thaI ncil fuuDII/mvnI mspl bstUI bstUI dsav bsh1236I bsh1236I nlaIV asuI taqI mnlI aciI hgaI aciI nlaIII cauII mnlI ·	FIG. 41L
	FIG
baofi hinpi hhal/cfol nlalv nari kasi hinll/acyl hgiCl haeli banl acil ahall/bsaHl 1 GATTGTAGGC GCGGCGTAT TGGAACAGAC	

fnu4HI

hphi fri pflMI avill/fspl styl bstUI bstII bstII bstUI				I							cac8I		_	/dra	bpml/gsul[dcm-] acil sfani bbvi ecool091/drall msll bmyl mnll caull-bfal acil 3601 CATCTCCAGC AGCCGCACGC GGCGCATCTC GGGCAGCGTT GGGTCCTGGC CACGGGTGCG CATGATCGTG CTCCTGTCGT TGAGGACCG GCTAGGCTGG GTAGAGGTCG TCGGCGTGCG CCGCGTAGAG CCCGTCGCAA CCCAGGACCG GTGCCCACGC GTACTAGCAC GAGGACAGCA ACTCCTGGGC CGATCCGACC
CATATCCA GTATAGG1				Idsm	hpall	BCTFI	ncii	dsaV	san96I			rmaI	mael	eco01091/drall	mnli cauli-bfal TCGT TGAGGACCCG AGCA ACTCCTGGGC
GCAG AA					Æ	380			<u>-</u> -	nlaIV	avall	asuI	IMndd		mnli ca STCGT TG CAGCA AC
pflMI styl bsli bsaJI ccca cccTTG									mbol/ndell[dam-]			pHI		THEAT	G CTCCT(
mstl pflMI aviII/fspI I bslI TG GGCAAACCAA AC GCGTTTGGTT								sau3AI	mbol/n	dpnI[dam+]	[dam-]	giAI/as	sp1286	avill/fspl bsiHKAI	MYI TGATCGT ACTAGCA
msti avili bsmi GAATG CG	H.] Iudp	hinPI dpnII[dam-]	hhal/cfol hgiAl/aspHI	mstI nlaIII bsp1286	aviII/f	nsli b Grece CP CACGC G1
b A ACTGTG F TGACAC	haeIII/palI mscI/balI	· H		dsaI	I			bsaJI	dcm+]		hinP		=		drall control
acil CTTGCGGAG/ GAACGCCTC7	hae	haeI	SCLFI	mval dsal	ecoRII	dsav	bstNI	bsll bsaJI	apyI[dcm+]	sau96I	lleva	asul eael	IWnda	nlaIV cfrI	ecool091/drall msll bmyl GGGTCCTGGC CACGGGTGCG CATGA7 CCCAGGACCG GTGCCCACGC GTACTA
CAATCAATT													fpu4HI	bsoFI	bbvI GGGCAGCGTT CCCGTCGCAA
nlaIV TTGGAG C									PI		voi		T/cfoI	aval	fani CATCTC CTAGAG
PflMI bsli ICCA AGAA? AGGT ICTI								fnudat	thai hinPi	PROFI	baoFI fnuDII/mvnI	batui	backt cackt hhal/cfol	bbvi acii bsh12361	acii s Sec eece See eece
I P ACCACTO										frudHT bsoFI	haoFI f	fnu4HT P	וווי ביי	r acir t	I (dcm-) AGCCGCAC ICGGCGIC
hphi tfii hinfi cggarr ca								٠				fund	1000	ppe.	bpmI/gsul[dcm-] acil sfaNI CTCCAGC AGCCGCACG GGCGCATC GAGGTCG TCGGCGTGCG CCGCGTAG
01 CTAAC GATTC															b 501 CATC GTAG
35															36

hgaI thaI aciI

hhaI/cfoI

3701 CGGGGTTGCC TTACTGGTTA GCAGAATGAA TCACCGATAC GCGAGCGAAC GTGAAGCGAC TGCTGCTGCA AAACGTCTGC GACCTGAGCA ACAACATGAA GCCCCAACGG ATGCACCAT GGTGGTTGTACTT GCTGGTTGTACTT GCCCCAACGG AATGACCAAT CGTCTTACTT AGTGGCTATG CGCTCGCTTG CACTTCGCTG ACGACGACGT TTTGCAGACG CTGGACTCGT TGTTGTACTT FIG. 41M

ddeI

maell

bsoFI bbvI

bsh1236I maeII

hinfi tfii

barI

fuuDII/mvnI

bstul

cac8I

thaI

fnu4HI bsoFI bbvI fnu4HI

```
3801 TGGTCTTCGG TITCCGTGTT TCGTAAAGTC TGGAAACGCG GAAGTCAGCG CCCTGCACCA TIATGTTCCG GATCTGCATC GCAGGATGCT GCTGGCTACC
                                                                                               ACCAGAAGCC AAAGGCACAA AGCATTCAG ACCTTTGCGC CTTCAGTCGC GGGACGTGGT AATACAAGGC CTAGACGTAG CGTCCTACGA CGACCGATGG
                                      fnu4HI
                                                       bsoFI
                                                                      bbvI
                            mrol bsaBI[dam-]
                                                              bspEI[dam-]
                hpall
                                             DSPMII
Idsm
                                                                   hhaI/cfoI
                                                 fnuDII/mvnI hinPI
                                                                bstuI
                   acil
                                 thaI
                                    TIOqu
                                                  PpuAI
                                                                   ppar
```

mbol/ndell[dam-]

sau3AI

mamI[dam-] dpnI[dam+]

dpnII[dam-]

bstYI/xhoII
alwI[dam-]

3901 CTGTGGAACA CCTACATCTG TATTAACGAA GCGCTGGCAT TGACCCTGAG TGATTTTTCT CTGGTCCCGC CGCATCCATA CCGCCAGTTG TTTACCCTCA GACACCTIGI GGAIGIAGAC AIAATIGCII CGCGACCGIA ACIGGGACIC ACIAAAAAGA GACCAGGGCG GCGIAGGIAI GGCGGICAAC AAAIGGGAGI fokī BfaNI acil acil **DamFI** 196nes nlaIV hhaI/cfoI cac8I hinpr tru91 haell

BCIFI

ncii

mspi

bsri hpaii

bsli dsav nlaiii

psp1406i maelii nspHi

CAACGTICCA GTAACGGGC ATGITCATCA TCACATA TCACAT

apol ball GTTGCAAGGT CATTGGCCCG TACAAGTAGT AGTCATTGGG CATAGCACTC GTAGGAGAGA GCAAAGTAGC CATAGTAATG GGGGTACTTG TCTTTAAGGG 001 CAACGITCCA GIAACCGGGC AIGITCAICA TCAGIAACCC GIATCGIGAG CAICCICICI CGITICAICG GIATCAIIAC CCCCAIGAAC AGAAATICCC

FIG. 41N

cac8I sau96I

sauyor tru9I haeIII/palI

asuI

msel

tru91

GGAATGIGCC ICCGIAGIIC ACIGGIIIGI CCIIIIIIGG CGGGAAIIGI ACCGGGCGAA AIAGICIICG GICIGIAAII GCGAAGACCI CIIIGAGIIG 4101 CCTTACACGG AGCCATCAAG TGACCAAACA GGAAAAAACC GCCCTTAACA TGGCCCGCTT TATCAGAAGC CAGACATTAA CGCTTCTGGA GAAACTCAAC bpmI/gsuI[dcm-] mseI acil bsli nlaili acil maeili moli

fouDII/mvoI hhaI/cfoI bstuI hinpi thal thaI fnu4HI **bsoFI** IlEdsu aluI IInad

fauDII/mvaI mnll bshl236I bstul fnu4HI **bsoFI** bcgI bbvI hinfi tfiI XmnI fnuDII/mvnI **bsh12361** bstul acil

4201 GAGCTGGACG CGGATGAACA GGCAGACATC TGTGAATCGC TTCACGACCA GGCTGATGAG CTTTACCGCA GCTGCCTCGC GCGATTTCGGT GATGACGTG CTCGACCTGC CTCGACCTGC GCCTACTTGT CCGTCTGTAG ACACTTAGCG AAGTGCTGGT GCGACATCC GAAATGGCGT CGACGGAGCG CGCAAAGCCA CTACTGCCAC acil bbvi bsh1236I hphI aluI m3]I asp700 aluI hgaI fokI

betul acil hinPI nspBII favm/IIdual hhaI/cfoI bsh1236I hqaI thaI drdI CauII hpall SCLFI Idem foki dsaV ncil sfani acil aluI maeIII esp31 bamBI DBMAI hpaII Idem Caull BCLFI nspHI aluI bslI ncil daav fpu4HI bsoFI bbvI nlaIII moli

1301 AAAACCICIG ACACAIGCAG CICCCGGAGA CGICACAGC TIGICIGIAA GCGGAIGCCG GGAGCAGACA AGCCCGICAG GGCGCGICAG CGGGIGIIGG TITIGGAGAC IGIGIACGIC GAGGGCCTCI GCCAGIGICG AACAGACAII CGCCIACGGC CCICGICIGI ICGGGCAGIC CCGCGCAGIC GCCCACAACC

FIG. 410

bsp1286 bsinkar	bmyl ndel	apaLI/snoI	alw44I/snoI	GAGTGCACC	CICACGIGG
	ddeI	rsal	csp61	GATTGTACTG A	CTAACATGAC T
sfanI	fnu4HI	bsoFI	acii	CONTRACTOR TO THE TOTAL ACTIVITY AND ACTIVITY ACCIDENT AND TAIL AND TAIL CONTRACT CONTRACT AND TAIL AN	CUCATALUS GOCCARCON INTERMITY NOTIFICATION TO TO TATORCOGNA TIGATACOCC GIAGICICGI CIAACAIGAC ICICACGIGG
		tru9I	mseI	CTT AAC	GAA TTG
		bst1107I tru9I	acil acci bsrl msel	GAGTGT ATACTGG	CTCACA TATGACC
			act	AT AGCG	TA TCCC
Toca	TILORE	bovi Find Tatt hert healt	ninki mimir bari bami hhar <i>iofo</i> r ethilirami	CCHALLY GUEL CACCOACTC ACGTAGGG	CTGGGTCAG TGCATCGC
fnu4HI	DSOF 1	bindt nist	bhar /cfor	TOUCHULA TO	CCGCGTCGGT A
					GCCCACAGCC

hqiAI/aspHI

mboli
earl/ksp6321 hinPI
sapl hhal/cfol
sfaNI hhal/cfol pleI bsoFl mcrI

acii acii bavi baiEI 501 ATATGCGGTG TGAAATACCG CACAGATGCG TAAGGAGAAA ATACCGCATC AGGCGCTCTT CCGCTTCCTC GCTCACTGAC TCGCTGCGCT CGGTCGTTCG

haeIII/palI b1 GCTGCGGCGA GCGGTATCAG CTCACTCAAA GGCGGTAATA CGGTTATCCA CAGAATCAGG GGATAACGCA GGAAAGAACA TGTGAGCAAA AGGCCAGCAA CGACGCCGCT CGCCATAGIC GAGIGAGITI CCGCCATTAI GCCAATAGGI GICTIAGICC CCTATIGCGI CCITICITGI ACACTCGITI ICCGGICGII TATACGCCAC ACTITATGGC GIGICTACGC ATTCCTCTT TATGGCGTAG TCCGCGAGAA GGCGAAGGAG CGAGTGACTG AGCGACGCGA GCCAGCAAGC ball cac8I haeI nlaIII aflIII IBdsu Idsu hinfI acil aluI acli barBI cacel fnu4HI bsoFI acil fnu4HI bsoFI bbvI

AAGGCCAGGA ACCGTAAAAA GGCCGCGTTG CTGGCGTTTT TCCATAGGCT CCGCCCCCT GACGAGCATC ACAAAAATCG ACGCTCAAGT CAGAGGTGGC TICCGGICCI IGGCAITIII CCGGCGCAAC GACCGCAAAA AGGIATCCGA GGCGGGGGA CIGCICGIAG IGIITITAGC IGCGAGIICA GICTCCACCG mplI drdI hgaI tagi sfani acil nlaIV cacBI fnuDII/mvnI haeIII/palI fnu4HI bsoFI acil **bsh1236I** batuI thaI balI apyI[dcm+] hacIII/palI haer nlaIV ecoRII bstNI SCIFI dsaV mvaI

FIG. 41P

						acti	CCTGTCCGC
				H	fnu4HI hpaII	bsoFI bsaWI	CGTTTCCCCC TGGAAGCTCC CTCGTGCGCT CTCCTGTTCC GACCCTGCCG CTTACCGGAT ACCTGTCCGC
				acil mspl	fuu4HI	bsoFI	ACCCTGCCG C
			psll)I	CCTGTTCC G
				PI	sSI	[dcm+] bsaJI aluI mnlI hhaI/cfoI	CGTGCGCT CI
		ы		hinPI	apy1[dcm+] bssSI	aluI molI	SAAGCTCC CT
SCLFI	mvaI	ecoRII	sav	bstNI	apyI[c	bsaJI	FICCCCC IG
	scrFI mv	mvaI	ecoRII dsaV	dsav bs	bstNI	apyI[dcm+]	TACCAGG CGT
							4801 GAMACCCGAC AGGACTATAA AGATACCAGG
							NCCCGAC AGG
							4801 GAN

CTTTGGGCTG TCCTGATAIT TCTATGGTCC GCAAAGGGGG ACCTTCGAGG GAGCACGCGA GAGGACAAGG CTGGGACGGC GAATGGCCTA TGGACAGGCG

alw44I/snoI apaLI/snoI 4901 CTTCTCCCT TCGGGAAGCG TGGCGCTTTC TCATACCTCA CGCTGTAGGT ATCTCAGTTC GGTGTAGGTC GTTCGCTCCA AGCTGGGCTG TGTGCACGAA GAAAGAGGA AGCCCTTCGC ACCGCGAAAG AGTATCGAGT GCGACATCCA TAGAGTCAAG CCACATCCAG CAAGCGAGGT TCGACCCGAC ACACGTGCTT **DSINKAI** bmyI aluI ddeI scfIaluI hhaI/cfoI hinPI haeII

hgiAI/aspHI

bsp1286

TANT CCM-1	fnu4HI	bsoFI	fnu4HI	bsoFI	bbvi maelli	bsrI bbvI bsrI
	Idsm	hpall	scrFI	ncil	dsaV	caulI
					plei	hinfI
			maelll	Idsm	bsaWI	of hpail
	fnu4HI	bsoFI	IIBdsu	acii hinPi	mcrI bbvI	bsiEI hhal/cfoI hpaII

001 CCCCCCGTTC AGCCCGACCG CTGCGCCTTA TCCGGTAACT ATCGTCTTGA GTCCAACCCG GTAAGACACG ACTTATCGCC ACTGGCAGCA GCCACTGGTA GGGGGGCAAG TCGGGCTGGC GACGCGGAAT AGGCCATTGA TAGCAGAACT CAGGTTGGGC CATTCTGTGC TGAATAGCGG TGACCGTCGT CGGTGACCAT

haeIII/pall maeI	acii scii naei naei biai	acaggattag cagagggagg tatgtagggg gtgctacaga gttcttgaag tggtgggccta actacggcta cactaggagg acagtatttg gtatctgggg
•	ñ	TATGTAGGCG GTGCTACAG
• • • • • • • • • • • • • • • • • • • •	TTUM	ACAGGATTAG CAGAGCGAGG

0

rmaI

bslI

FIG. 41Q

nlaIII DapHI rcal 5301 ATTACGCCCA GAAAAAAGG ATCTCAAGAA GATCCTTTGA TCTTTTCTAC GGGGTCTGAC GCTCAGTGGA ACGAAAACTC ACGTTAAGGG ATTTTGGTCA TAAIGCGCGT CITITITCC TAGAGITCTI CTAGGAAACT AGAAAAGAIG CCCCAGACTG CGAGICACCI IGCITIIGAG IGCAAIICCC IAAAACCAGI 5201 TCTGCTGAAG CCAGTTACCT TCGGAAAAAG AGTTGGTAGC TCTTGATCCG GCAAACAAAC CACCGCTGGT AGCGGTGGTT TTTTTGTTTG CAAGCAGCAG AGACGACTIC GGICAAIGGA AGCCIITIIC ICAACCAICG AGAACIAGGC CGITIGIIIG GIGGCGACCA ICGCCACCAA AAAAACAAAC GIICGIGGIC fnu4HI **bsoFI** bbvI cac8I tru9I mseI maell acil nspBII acil hgal ddel mboI/ndeII[dam-] dpnII[dam-] alwI[dam-] dpnI[dam+] mbol/ndeII[dam-] hpall Idem sau3AI dpnII[dam-] mboII[dam-] dpnI[dam+] mboI/ndeII[dam-] sau3AI aluI dpnII[dam-] alwI[dam-] dpnI[dam+] alwI[dam-] bstYI/xhoII gau3AI mbol/ndeII[dam-] dpnII[dam-] bstYl/xhoII dpnI[dam+] maeIII eco571 bsrI fuuDII/mvaI hhaI/cfoI **bsh1236I** hinpi bstuI thaI

ahaIII/draI tru9I msel tru9I msel ahaIII/draI mbol/ndeII[dam-] tru9I msel dpnII[dam-] bstYI/xhoII bstYI/xhoII alwI[dam-] dpnI[dam+] sau3AI mbol/ndell[dam-] alwI[dam-] bfaI mael rmaI mpoII[dam-] dpnII[dam-] hphI dpn I [dam+]

5401 TGAGATTATC AAAAAGGATC ITCACCIAGA ICCITITAAA ITAAAAAIGA AGITIIAAAT CAAICIAAAG IAIAIAIGAG IAAACIIGGI CIGACAGIIA ACTCTAATAG TITITCCTAG AAGTGGAICT AGGAAAATT AATTITTACT TCAAAATTTA GTTAGATTTC ATATATACTC ATTIGAACCA GACTGTCAAT sau3AI nlaIV

mbol/ndeII[dam-]

hgiCI bani

tru9I

dpnI[dam+]

501 CCAATGCTTA ATCAGTGAGG CACCTATCTC AGGGATCTGT CTATTTCGTT CATCCATAGT TGCCTGACTC CCCGTCGTGT AGATAACTAC GATACGGGAG GGTIACGAAT TAGTCACTCC GTGGATAGAG TCGCTAGACA GATAAAGCAA GTAGGTATCA ACGGACTGAG GGGCAGCACA TCTATTGATG CTATGCCTC ahdI/eam1105I fokI dpnII[dam-] ddeI mnlI mseI

pleI hinfI

FIG. 41R

Io		m _]
haeIII/palI gau96I hinPI asuI hhaI/cfoI GGGCCGAGC	maell cfol ssp14061 fsp1 AACGT	<pre>sau3AI mbol/ndeII[dam-] dpnI[dam+] dpnII[dam-] II nlaIII alwI[dam-]</pre>
haeIII/pulI Bau96I hinPI asuI hhaI/ GGGCCGAGC CCCGGCTCG	maell hinPl hhal/cfol mstl psp1406I avill/fsp1 TGCGCAACGT	sau3AI mboI/ndeII[dam+] dpnI[dam+] dpnI[dam+] dpnI[dam+] dpnI[dam+] dpnI[dam-] maeIII alwI[dam-]
mspi hpali ogli e scccca AC)	m-] nla naeIII
msp hpa bglI cac81 GCCAGCCG	tru9I bsrI mseI cca GTTAAT	sau3AI mbol/ndeII[dam-] dpnI[dam+] dpnII[dam-] maeI
AAACCA	bsr] TCGCCA	sau3AI mbol/ndeII dpnI[dam+]
G CAAT!	G TAGT	
[dcm-] [TTATCA	aI aI AGAGTAA	nlaIV mspI bsaWI aluI hpaII
bpmI/gsuI[dcm-] I I/bsrFI aIV crcca GATTTATCA	rmal mael bfal alul AAG CTAG	b
bpm1/gs: msp1 hpal1 cfr101/bsrFI hph1 nlalV rC ACCGCTCCA G	scrFI ncil mspl hpalI dsav caulI rspl	
o hphi cgcrc A	scrF ncil mspi hpar tru91 dsaV msel caul asel/asnI/vspi ATTAATTGT TGCCGG	
AI I /mvnI 6I : TGGGTC	tru9I mseI aseI/a TATTAAT	
bsmAI bsaI thaI fnuDII/mvnI bstUI bsh1236I aciI ccGCGAG ACCC	bsrI fokI CATCCAGTC	
I TG ATA	mnll I fo CCT CCA	maeili
bsrl fau961 fnu4HI nlaiV bsoFl haeIII/pall bsrbI asul bbvI GGCCCCAG TGCTGCAAT	mn acii TATCCGCC	
bsrl 61 f V b II/pall	AACT T	BI mell sfani
bs: sau961 nlaIV haeIII asuI crcccccc	Bau96I avaII asuI GG TCCTGC	cac8I scfI pstI fnu4HI bsoFI bbvI
bsal bsal bsal thal thal sau96I fnu4HI fnuDII/mvnI mspI nlaIV bsoFI bstUI cfrl0I/bsrFI haeIII/pall bsrDI acil hphI nlaIV cac81 soughtian contanance georgecong Tecrecong Tecreco	scrFI ncil msp1 hpall rmal hpall rmal hhal/cfol avall asul acil fokl asel/asnl/vsp1 alul acil fokl asel/asnl/vsp1 alul bsrI msel avill/fsp1 acil fokl asel/asnl/vsp1 alul acil fokl asel/asnl/vsp1 alul bsrI msel avill/fsp1 acil fokl asel/asnl/vsp1 alul bsrI msel avill/fsp1 acil fokl asel/asnl/vsp1 alul bsrI msel avill/fsp1 accrecacacacacacacacacacacacacacacacacac	barDl
1 GGCT1	1 GCAG	
	0	

fnu4HI bsoFI bbvI nlaIII malI hacIII/palI fnu4HI bsoFI acil eaeI cfrI mbol/ndeII[dam-] mnll dpnII[dam-] dpnI[dam+] sau961 pvul/bspCI gau3AI bsiEI MCrI avall asuI aluI acil

TGTTGCCAIT GCTGCAGGCA TCGTGGTGTC ACGCTCGTCG TTTGGTATGG CTTCATTCAG CTCCGGTTCC CAACGATCAA GGCGAGGTTAC AKGATCCCCC ACAACGGTAA CGACGTCGT AGCACCACAG TGCGAGGGGG AACCATACC GAAGTAAGTC GAGGCCAAGG GTTGCTAGTT CCGCTCAATG TACTAAGGGGG

barDI bagI sfaNI

ATGITGIGCA AMAMAGCGGI TAGCICCTIC GGICCICCGA ICGITGICAG ANGIANGIIG GCCGCAGIGI IAICACICAI GGITAIGGCA GCACIGCAIA TACAACACGI IIIIICGCCA AICGAGGAAG CCAGGAGGCI AGCAACAGIC IICAIICAAC CGGCGICACA AIAGIGAGIA CCAAIACCGI CGIGACGIAI

FIG. 41S

mcrI bsiEI bcgI

fnu4HI

rsal

scal

bsrI

fokI

bsoFI ddeI acil

TAAGAGAATG ACAGTACGGT AGGCATICTA CGAAAAGACA CTGACCACTC ATGAGTIGGT TCAGTAAGAC TCTTAICACA TACGCCGCTG GCTCAACGAG 001 ATTCTCTTAC TGTCATGCCA TCCGTAAGAT GCTTTTCTGT GACTGGTGAG TACTCAACCA AGTCATTCTG AGAATAGTGT ATGCGGCGAC CGAGTTGCTC maelli hphi csp61 sfani nlaIII

mbol/ndell[dam-] dpnII[dam-] bstYI/xhoII dpnI[dam+] alwI[dam-] sau3AI Iloqu psp1406I maell asp700 XnnnI hgiAI/aspHI bsp1286 **DSIMKAI** bmyI ahalii/drai tru9I msel funDII/mvnI hhaI/cfoI **bsh1236I** hinPI bstuI thal acil cauli hincil/hindil ahaII/bsaHI hinlI/acyI hqaI hpaII Idem SCLFI ncil dsaV

pi teccegece tcaacacege ataatacege gecacatage agaactitaa aagtecteat cattegaaaa egtetteeg gecgaaact etcaaggate AACGGCCCC AGTIGICCC TAITAIGGCG CGGIGIAICG ICIIGAAAII ITCACGAGIA GIAACCIITI GCAAGAAGCC CCGCIITIGA GAGIICCIAG

mbol/ndell[dam-] mpoII[dam-] sfaNI eco57I dpnI[dam+] sau3AI alw44I/snoI hqiAI/aspHI apaLI/snoI **bsp1286 DSIHKAI** bmyI mpol/ndell[dam-] taqī dpnII[dam-] dpnI[dam+] alw[[dam-] barI gau3AI

TIACCGCTGT TGAGATCCAG TICGATGIAA CCCACTCGTG CACCCAACTG ATCTTCAGCA TCTTTTACTT TCACCAGCGT TTCTGGGTGA GCAAAAACAG AAIGGCGACA ACTCTAGGIC AAGCIACAII GGGIGAGCAC GIGGGIIGAC IAGAAGICGI AGAAAAIGAA AGIGGICGCA AAGACCCACI CGIIIIIGIC hphI hphI dpnII[dam-] bassI maelll bstYI/xhoII

IIBqen

Iloqu Enu4HI acii

sspI

earI/ksp632I

mslI

bsoFI

GAAGGCAAAA IGCCGCAAAA AAGGGAAIAA GGGCGACACG GAAAIGTIGA AIACICAIAC ICTICCITIT ICAAIAIIAI IGAAGCAIII AICAGGGIIA CTICCGITII ACGGCGIIII IICCCIIAII CCCGCIGIGC CIIIACAACI IAIGAGIAIG AGAAGGAAAA AGIIAIAAIA ACIICGIAAA IAGICCCAAI FIG. 411

ahaII/bsaHI aatii ddei hinl1/acyl maell plaiv hhai/cfoi fnuDII/mvnI **bsh1236I** bstul acil mboII bpuAI eco01091/draII haeIII/palI sau96I asaI mnll tru9I nlaIII bspHI acil bsmAI bsrBI nlaIII rcal

hinPI

thaI

FIG. 41U

6501 ACCATTATTA TCATGACATT AACCTATAAA AATAGGCGTA TCACGAGGCC CTTTCGTCTT CAA $(S \in \mathcal{U} \cup \mathcal{NO} \cup \mathcal{O})$ TGGTAATAAT AGTACTGTAA TTGGATATTT TTATCCGCAT AGTGCTCCGG GAAAGCAGAA GTT

bapHI rcal

Isqq

>length: 6563

```
1119 1195 1425 1434 1446 1512 1695 1696 1752 2155 2375 2727 3002 3090 3339 3463
                                                                                                                                                           3436 3448 3490 3544 3597 3613 3619 3700 3838 3967 3970 3981 4139 4155 4210 4266
                                                                                                                                                                                                                                                                                                                                                                                                                                                     2218 2233 2889 3292 4202 4259 4270 4319 4338 4619 4845 4935 4981 5238 5759 5859
                                                                                                                             2628 2781 2784 2787 2906 2926 3005 3045 3094 3141 3226 3241 3309 3342 3367 3412
                                                                                                                                                                                      4351 4390 4400 4442 4467 4505 4518 4544 4561 4604 4611 4632 4723 4751 4878 4897
                                                                                                                                                                                                                                                                                                                                                                                                                           72 121 252 320 398 532 589 648 1126 1144 1167 1325 1386 1906 2054 2075 2126
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          412 413 712 713 1171 1471 2578 2579 3300 3870 5245 5319 5331 5416 5429 5893
                                                                                                   178 542 805 877 1340 1750 1826 2011 2039 2043 2182 2242 2384 2492 2501 2504
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       640 999 1347 1357 1449 1665 1713 1755 1764 2333 3262 3645 4705 4826 4839
                                                                                                                                                                                                                  5018 5128 5263 5272 5634 5725 5916 5962 6083 6127 6204 6313 6412 6459
                                                                                                                                                                                                                                                                                                                                           1645 1813 2616 2637 2751 3408 6107 6489
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    1831 4494 4992 6238
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     1831 4494 4992 6238
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 905 930 4234 6166
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            alwNI[dcm-](CAGNNNCTG): 1117 1385 5089
                                                                                                                                                                                                                                                                                                                                                                           5435 5454 6146
                                                       1093 1963 4449
                                                                                                                                                                                                                                                                                                                                                                                                       ahdI/eam11051(GACNNNNNGTC): 346 5566
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        see tthlllI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   1 391 4093
                                                                                   3867[dam-]
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            see hglAI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    6196 6214
                                                                                                                                                                                                                                                              see hinli
                                                                                                                                                                                                                                                                                          1307 4678
1645 6489
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           see aseI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  403 823
                           403 823
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            1695
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             5742
                                                                                                                                                                                                                                                                                                                        1788
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 5922
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           asel/asnl/vspl(ATTAAT):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          alw441/snoI(GTGCAC):
                                                                                                                                                                                                                                                                                                                                                                             ahaIII/draI(TTTAAA):
                                                                                                                                                                                                                                                                                                                                                     ahaII/bsaHI(GRCGYC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         apaLI/snoI(GTGCAC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       asp700 (GAANNNTTC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        alwI[dam-](GGATC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               apyI[dcm+](CCWGG):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  asp718 (GGTACC):
                               acc651 (GGTACC):
                                                                                       accIII (TCCGGA):
                                                                                                                                                                                                                                                                                              aflii(ACRYGT):
   aatii(GACGTC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     apol(RAATTY):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            apal(GGGCCC):
                                                             acci (GTMKAC):
                                                                                                                                                                                                                                                                                                                          ageI(ACCGGT):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        asuI (GGNCC):
                                                                                                                   acil(CCCC):
                                                                                                                                                                                                                                                                                                                                                                                                                                             aluI(AGCT):
```

FIG. 41V

Stop Template Primer

5' CAT GGT ATA GGT TAA ACT TAT TTA CAC 3' (SEA ID NO: 63) SL.97.2

5' CAT GGT ATA GGT NNS ACT TAT TTA CAC 3' (SEQ ID NO: 64) NNS Randomization Primer SL.97.3

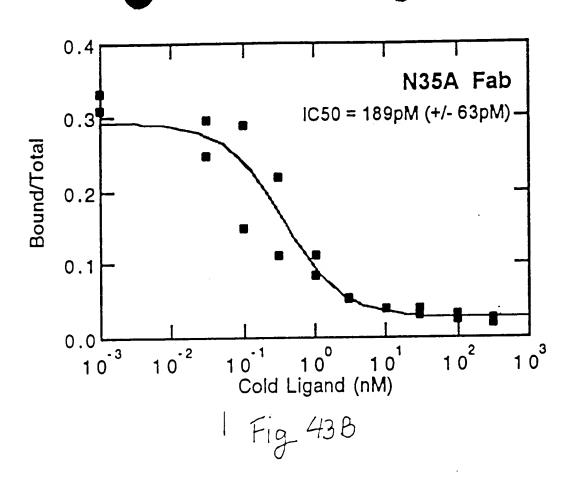
FIG. 42

Randomization of Position N35 of Variable Light Chain CDR-1 Amino Acid Frequency

Phage Display (NNS Codon Library) Sort #3

IC50 (nM)	4.9	3.1	3.1	0.1	0.2	ND	ND .
% Total	5.6	16.6	16.6	22.2	5.6	5.6	1.9
Frequency % Total		9	3	4	2		
Amino Acid	Asparagine (wt)	Glycine	Aspartic Acid	Glutamic Acid	Alanine	Lysine	Serine

FIG. 43A



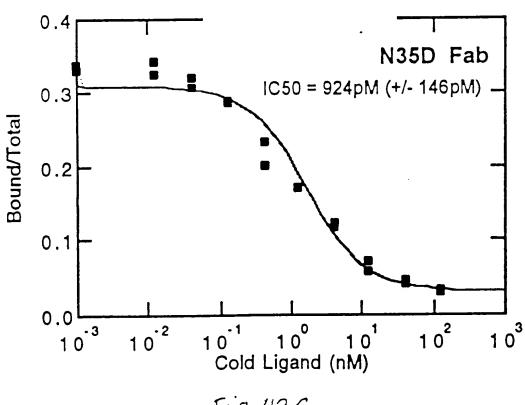
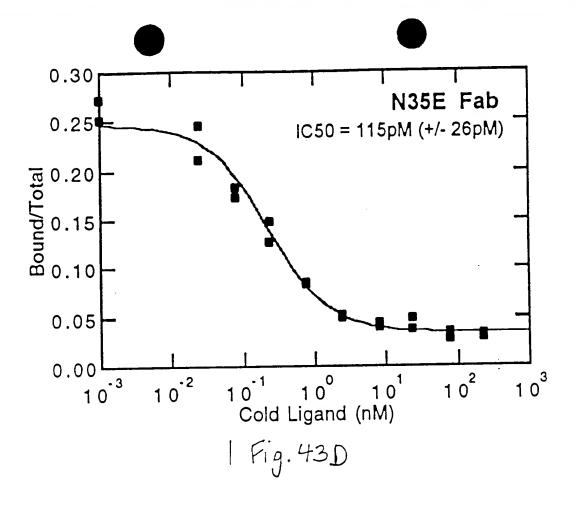
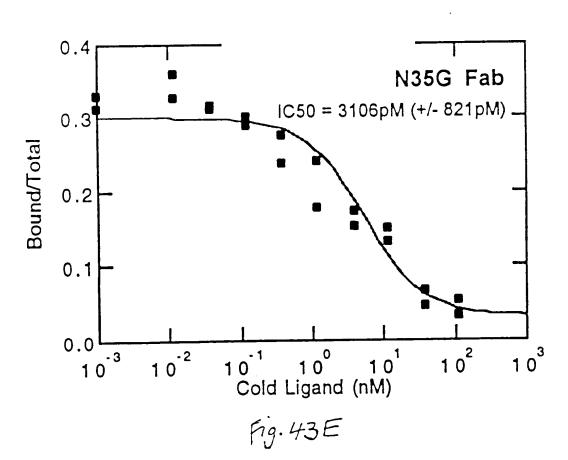
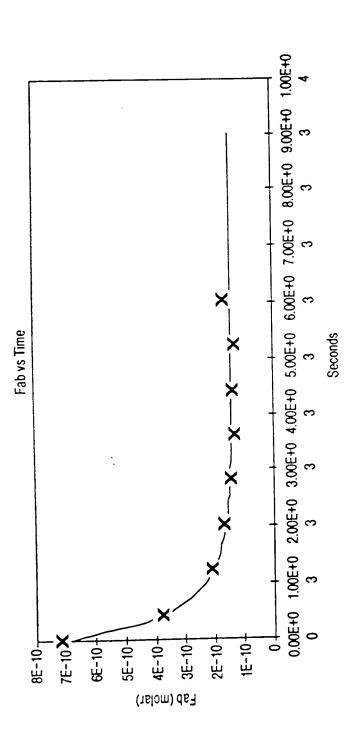


Fig. 43C







Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.F(ab')2.

SAMPLE	ka	kd	Kd
6G4V11N35A-Fab	QN	QN	114pM
6G4V11N35A-F(ab') ₂	$2.0x10^6$	$2.1x10^{-4}$	109pM
6G4V11N35E-Fab	4.7×10 ⁶	2.6x10 ⁻⁴	54pM

FIG. 44

•	ATGAA	22202	\ h m	ነ ጥር	CAS	. بلغا	لملك	لملات	YGCA	TCI	'ATG	TT	CG	TTTTT	TCI	TAT	TGCI	CACA	LAAC	
	m > 0 mm	*****	מים יי	TAC	CCT	4 4	ACAB	CADA	CGT	AGA	TAC	'AAC	3C	AAAAA	LAGA	YI'A	MCGF	1101	110	
	M K	TITC	L LA	TAG	N 1	74 E	AGA. T.	T.	Δ	s.c.	M	F	V	F	S	I	A	T	N	
-23	M K	Kr	4	Ι.	A 1	•	ם	ם	^	_	••	•								
	GCATA				~ . ~ .		~ \ C		·TCC	ccc	יאכר	·TC	~~	ጥርጥር	GCC	TC	TGTO	GGG	GAT	
61	GCATA CGTAT	CGCT	S AT	ATC	CAG	AT.	GACC	CAC	,100	220	, MOC	120		ACAGO		DAG	ACAC	ccc	CTA	
	CGTAT	GCGAG	CTA	TAG	GTC'	ГА	CTGC) [انی -	AGG	GGC	.100	, A.G.	•	ACAG	, C.O.	27.0	v	G	D	
-3	A Y	A I)	I	Q 1	M	T	Q	S	Р	S	5	L	3	^	3	•	•		
														3 maga	n s m	100	ጥና እር	2000	ידעריב	
121	AGGGT	CACC	A TC	:ACC	TGC.	AG	GTC	AAGI	CAA	AGO	CTTA	\GT	AC	ATGG	CAL	RCC	TON	2MC(מחמר	
	TCCCA	GTGG!	r Ac	TGG	ACG'	TC	CAG	MC	GTT	TCC	GAA?	CA'	TG	TACCA	ATA	ICC	AC I	- 1 G (-WIV	
18	R V	T	I	T	C ;	<u>R_</u>	S	<u>\$</u> _	<u> </u>	<u>s_</u>	<u> L</u> _	<u>v_</u>	_H_	G	_1_	<u>. G</u>				
121	TTACA	ירתכים,	r an	CAA	CAG	AA	ACC	AGG?	AAA	GC:	rcco	SAA	AC	TACTY	SAT	TTA	CAA	AGT	ATCC	
	מיצית ת	YEACC!	አ ጥጀ	CTT	STO	LaL	TGG	rcc:	LLLL	CGZ	AGG($\mathbb{C} T \cdot \Gamma$	TG	ATGA	-TA	AAT	GII	ICM	1400	
20	L H	1.1	v	0	0	т- К	P	G	ĸ	A	P	K	L	L	I	Y	K	<u>-Y</u> _	S	
38	11 11	ν.	1	v	~	•	•	•										•		
	AATCO		_ ^_	~~~	C/D/C		بالملك	TCC	-بلحك	ΨC	י בי בי	እጥር	CG	GTTC'	TGG	GAC	GGA'	TTT	CACT	
241	AATC	SATIC	T CI	IGGA	(G1C		110	2000	27.70	J.C.	יים בי זיים ל	ראכ	GC.	CAAG.	ACC	CTG	CCT	AAA	GTGA	
	TTAG	TAAG.	A GA	ACCT	'CAG	نىي	AAG.	AGC	SAAG	AG.	ACC.	יאפ	~	cano.	G	T	מ	F	T	
58	N R	_F	<u>s</u>	G	V	P	S	R	r	5	G	3	G	3	•	•	_	•	•	
																mmc.	202	CAC	מש כת	
301	CTGAC	CATC	A GO	CAGT	CTG	CA	GCC.	AGA	AGAC	TT	CGC.	AAC	TT	ATTA	CIG	110	ACA	GAG	IACI	
	CACTO	CTAC	T C	מ שת:	CAC	CT	CGG	TCT	TCTG	AA	GCG'	${ m TTG}$	AA	TAAT	GAC	AAG	101	CIC	AIGA	
78	L T	Ī	S	S	L	Q	P	Ε	D	F	Α	${f T}$	Y	Y	С	<u>s_</u>	0_	_S_	_ <u>T</u>	
2 6 1	CATG	~~~~~	C Tr	- N C C	لملمك	22	ACA	GGG'	TACC	AA	GGT	GGA	GA	TCAA	ACG	AAC	TGT	GGC	TGCA	
			C 3/	~m~~	* A A A	CC	TYTH	CCC	Y TYCE	للملك	CCA	CCT	CT	AGTT	160	116	ALA	$\mathcal{L}_{\mathcal{L}_{\mathcal{L}_{\mathcal{L}_{\mathcal{L}}}}}$	MCGI	
	H V	AGGGC	G A	ر س	-844	.cc	191	CCC.	T C C	ĸ	v	E	T	K	R	T	v	Α	Α	
98	<u>HV</u>	P	Ь	<u>-1'</u>	r	G	Ž	G	1		•	_	-	•	•	_				
										٥,	~~`	cmt	~ 3	8 8 TO	т ~-С	יא אר	TCC	الميل.	. עריטעי	
421	CCAT	CTGTC	T T	CATO	CTTC	CC	GCC	ATC	TGAT	GA	GCA	GIT	.GA	MAIC	300		200	מממ		
	GGTA	GACAG	A A	GTAC	SAAC	GG	CGG	TAG	ACTA	CT	CGT	CAA	(CT	TTAG	ACC	.110	ACG	امم	V	
118	P S	V	F	I	F	P	P	S	D	Ε	Q	Ъ	K	S	G	1	А	3	•	
				•													CCT	~~ x	ma a c	
481	GTGT	GCCTG	C D	GÀA!	PAAC	TT	CTA	TCC	CAGA	GA	.GGC	CAA	\AG	TACA	GTC.	GAA	GGI	COM	TAAC	
	C3 C3	~~~~	C 1	زيلمك	YTT	445	GAT	ኒልርር	GTCT	' CI	'CCG	GTI		AIGI	CAC	11	CCA	ι	AIIG	
138	V C	Ţ,	L	N	N	F	Y	P	R	Ε	Α	K	V	Q	W	K	V	Ð	N	
5/1	GCCC	ጥርር እ ፤	יה כ	GGG'	TAAC	CTC	CCA	GGA	GAGT	GI	CAC	AGA	AGC	AGGA	CAC	CAA	GGA	CAC	CACC	
	0000	N C C TY	רא כ	CCC	ALAL V	באכ	ഭദേ	$^{\circ}$ CT	CTCA	CP	GTC	TU	1,00	TUCT	C T C	-611	CC 1	. 616	.0100	
150	A L	WGG 1 1	יא ס	~ CCC.	N	50	0	F	S	v	Т	E	0	D	S	K	D	S	T	
158	AL	Ų	3	G	**	J	×	_	_	-	_		_							
	TACA				~ > ~	- C M	CNO		~ > C	. 7.7	ACC	יאכו	۵СТ	ACGE	GAZ	AACA	CAA	AGI	CTAC	
601	. TACA	GCCT(CA G	CAG	CAC		GAC	2001	CONC		****	, TO 1	ע באר	TGCT	ملاک - ۱۵۰	THOT	CIL	TC	GATG	
	ATGI	CGGAC	GT C	GTC	GIG	GGA	CIC	ع في) و -	CICC	, 1,	1100	2 T.C.	A	1001	· · ·	น	ĸ.	v	Y	
178	ATGT S Y S	L	S	S	${f T}$	L	T	L	S	K	Α	ע	I	E	7	n	K	•	•	
661	L GCCI	CCGA	AG I	CAC	CCA'	TCA	GGG	GCC1	rGAGC	T	CGCC	CG'	TCA	CAA	AGA(11) 	CAA	ACAC	ACCCE.	
		0000	T~ >	CTC	CCT	ACT	י ררנ	າດດະ	1 CTCC	: A(GCGC	3GC/	AGI	GILL	$\Gamma \subset \Gamma_1$	JUAA	, G.	101		
109	CGGA 3 A C	E	v	Т	Н	Q	G	L	S	S	P	V	1	K	S	F	N	R	G	
100	, n ,		•	-	-	-														1.51.50 12.45
77	י כאכי	وبلعلتك	אה ר	TCA	TCC	тст	ACC	SCC	GACC	s c	ATC	GTG	GCC	CTA	STA	CGCA	AC:	rag'	rcgta	(६६६ क) १८०१ ६५
12.	י פאט ז	ער ע ט <i>י</i>	TY (ZACT	יאַככ	AGA	TG	CGG	CTG	G G	rag	CAC	CGG	GAT	TAC	GCGI	TG	ATC	AGCAT	
~	B E	CAAI	1581	(T)	WO:	62)	'												
218	5 E ((~~			-													

FIG. 45

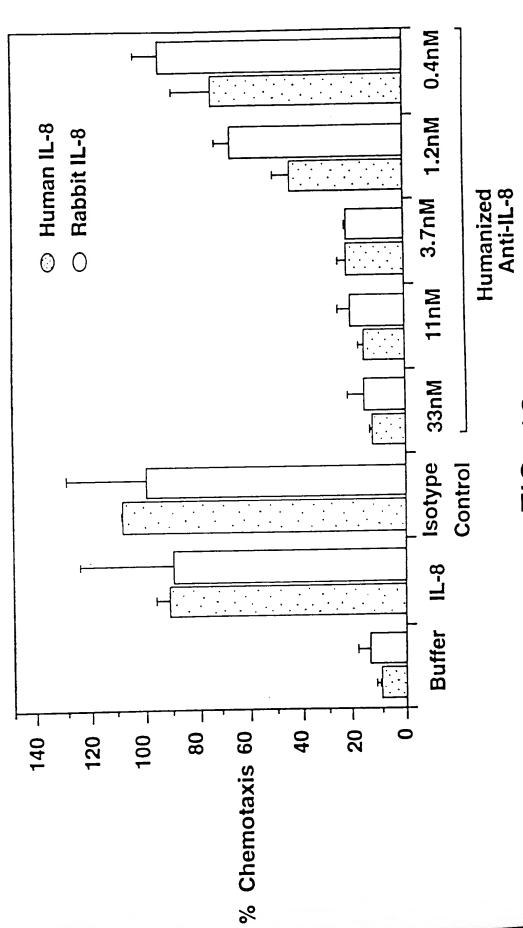


FIG. 46

N35AH1upr

N35AH11wr

5-TCGAGAGGAGTAGCCAGAAGCTGCACAGGACAAACGGAGTGAGCCCCCTGGCTGCACCAGGCCACCGCCAGACTGCACT AG-3'

Bold indicates nucleotide change destroying Pvull site.

FIG. 47

>This has the pSVI backbone with the pRK7 cloning linker (pSVI7) and the intron DHFR(ID) >made from pSVI.WTSD.D by adding a linearization linker(LL) into the Hpal site > length: 8120 (cfrcular)

apyI [dcm+] nlaiv ecoRII bstNI scrFI bsaJI dsav MV&I DSmFI mbol/ndell[dam-] nspBII hinf! tagl[dam-] pvull sau3AI aluI pleI dpnII[dam-] dpnI[dam+] pvuI/bspCI tadI[dam-] bsiEI mcrI bfal rmaI maeI hgiAI/aspHI ecl136II cacel **bsp1286 DS1HKAI** hgiJII banII aluI bmyI saci sstI

1 ITCGAGCICG CCCGACATIG ATTATIGACI AGAGICGAIC GACAGCIGIG GAAIGIGIGI CAGITAGGGI GIGGAAAGIC CCCAGGGCICC CCAGCAGGCA AAGCICGAGC GGGICGIAA TOICAGCIAG CIGICGACA CITACACACA GICAAICCCA CACCITICAG GGGICCGAGG GGICGICGI

nsiI/avaIII nspHI cac8I sfani ppu10I nlallI cac8I apyI[dcm+] bsmFI nlaIV ecoRII bsaJI bstNI dsav mval apy1[dcm+] ecoRII scrFI bstNI dsav sexAI mvaI nsil/avallI stani ppu101 nlaIII nspHI cac8I Idsu SphI

101 GAAGTATGCA AAGCATGCAT CTCAATTAGT CAGCAACCAG GTGTGGAAAG TCCCCAGGCT CCCCAGCAGG CAGAAGTATG CAAAGCATGC ATCTCAATTA CITCATACGI ITCGTACGIA GAGITAATCA GICGIIGGIC CACACCITIC AGGGGICCGA GGGGICGICC GICTICATAC GITICGIACG IAGAGITAAI

nlalil

styI ncoI acil deal acil fokl acil beaJI

acil

201 GTCAGCAACC ATAGTCCCGC CCCTAACTC GCCCTTCCG CCCCTAACTC CGCCCAGTTC CGCCCATTCT CCGCCCCATG GCTGACTAAT TTTTTTATT CAGTCGTTGG TATCAGGGCG GGGTTGAGG CGGGGTTGAG GCGGGGTAAGA GGCGGGGTAC CGACTGATTA AAAAAAATAA **bsmFI**

FIG. 48A

haeIII/pall mcri eagl/xmaIII/eclXI eael cfrI baiEI cpl		
haeIII/palI uI mcrI eagl/xmaIII/ eaeI cfrI baiEI mspI hpaII GCTTATCGG	nlalli ATGTACCA	real cepéi scal CAAGTACTTC GTTCATGAAG
aluI mcr. rmal eagimael bfal cfr. nhel bell alul hpal CAAAAAGCTA GCTTATCGGG	fnu4HI bsoFI bbvI nspBII aclI nTCCCGCTG CCATCA	xmnI asp700 GGACGAGTT CA
rmal maci styl bsayl bsayl bsayl bhall avril[dam-] haelil/pall stul mnll stul hael bseRl AGAGGTTT TTTGGAGGC TAGGTTTTG TCTTCATCAC TCCTCCGAAAAC	fnu4HI bsoFI bsoFI csp[]	haeIII/palI haeI scrFI mvaI bsrBI ecoRII dsaV bsmAI apyI[dcm+] bsaI bsaJI mnlI ddeI GGGATTGCCA AGAACGAGA CCTACCCTGG CCTCCGCTCA CCCTAACCGT TCTTGCCTCT GGATGGCACT
mnli bseRI G AGGAGCTTT TTTG	*	bsmal bsal ccctaaccet tettgeetet gga
	maell maelli G AGTGACGTAA	
fnu4HI bsoFI bglI sfiI haeIII/palI mnll mnll ddeI mnll bsaJI mnll aluI mnll bsaJI acil haeIII/palI ATACGCGGC CCGGGCG CTCGCCTCT GAGCTATTCC ATACGTCTC GGCTCCGGCG GAGCCGAGA CTCGATAAGG	tfii hinfi acii thai fnuDiI/mvni bstUi bsh1236i cGCGGATTCC CCGTGCCAAG	pflMI bslI TCGACCATTG AACTGCATCG TCGCCGTGTC CCAAAATATG AGCTGGTAAC TTGACGTAGC AGCGGCACAG GGTTTTATAC
fnu4HI baoFI baoFI sfiI sfiI haeIII/palI haeIII/palI baJI mnlI baJI acil h	scrFI nc1I mspI hpaII dsaV cauII CCGGAACGC TGCATTGGAA GGCCTTGCC ACGTAACCTT	taqi TCGACCATTG AACTGCATCG AGCTGGTAAC TTGACGTAGC
h mnl 301 TATGCAGAG ATACGTCTC	scrFI nc1I mspI hpaII dsaV cauII 01 CCGGAACG	taqi 1 TCGACCATI AGCTGGTA

FIG. 48B

ahalll/dral tru91 701 AGACAGAAT TAATATAGIT CTCAGTAGAG AACTCAAAGA ACCACCACGA GGAGCTCATT TTCTTGCCAA AAGTITGGAT GATGCCTTAA GACTTATTGA TCCTGTCTTA ATTATATCAA GAGTCATCTC TTGAGTTTCT TGGTGGTGCT CCTCGAGTAA AAGAACGGTT TTCAAACCTA CTACGGAATT CTGAATAACT 601 CAAAGAATGA CCACAACCTC TTCAGTGGAA GGTAAACAGA ATCTGGTGAT TATGGGTAGG AAAACCTGGT TCTCCATTCC TGAGAAGAAT CGACCTTTAA mseI GITICTIACT GGTGTTGGAG AAGTCACCTT CCATTTGTCT TAGACCACTA ATACCCATCC TTTTGGACCA AGAGGTAAGG ACTCTTCTTA GCTGGAAATT aflii/bfri ddel mboli tagi tru9I hinfi foki sfani msei apy1[dcm+] betXI betni dsav **6exAI** hgiAI/aspHI ecl136II **bsp1286 DSIHKAI** hqiJII mnll aluI bessi banii bmyI sstI saci bseRI hinfi hphi ball alwNI [dcm-] tfil ear1/ksp6321 eco571 Iloqu asel/asnl/vspl mnll tru91 mseI

ecoRII

BCrFI

mval

naeIII/palI haeI

ecoRII BCLFI dsav tfil ecoRII dsav BCLFI mvaI

ddel plel apyl[dcm+] hinfl apyl[dcm+] **b**stNI nlaliI bstNI

hinfi

TGITGGCCIT AACCGITCAI IICAICIGIA CCAAACCIAI CAGCCICCGI CAAGACAAAT GGICCTICGG IACITAGIIG GICCGGIGGA AICIGAGAAA 801 ACAACCGGAA TIGGCAAGIA AAGIAGACAI GGITIGGAIA GICGGAGGCA GIICIGTIIA CCAGGAAGCC AIGAAICAAC CAGGCCACCI IAGACICIIT

mnlI

accI nlallI

hpall DRAWI

MBPI

FIG. 48C

mnlI ball ddel 901 GIGACAAGGA ICAIGCAGGA AITIGAAAGI GACACGITIT ICCCAGAAAI IGATITIGGG AAATATAAAC CICICCCAGA ATACCAGGG GICCITITA CIAAACCC ITTATATITIG GAGAGGGTCI TAAGGGICG CAGGAGAGAC CAGGAGAGAC ecoNI mnlI apyI[dcm+] ecoRII BCLFI beaJI betNI BVaI dsav mn l I maell aflili maelii mbol/ndell[dam-] maeIII alwi[dam-] apoi dpnII[dam-] dpnI[dam+] nlaIII 8au3AI

aha II BaaHI

hinli/acyi

hqaI

1001 AGGICCAGGA GGAAAAAGGC ATCAAGTATA AGTITGAAGI CTACGAGAAG AAAGACTAAC AGGAAGAIGC ITICAAGTIC ICTGCICCCC ICCTAAAAGCI ICCAAGGICCI CCIIITIICCG IAGIICAIAI ICAAACTICA GAIGCICTIC ITICIGAIIG ICCITCIACG AAAGIICAAG AGACGAGGG AGGAITICGA mnlI Iloqu sfani Ilodm acci BfaNI apyI[dcm+] Ilum ccoRII betNI BCLFI dsav mva] Bau96I avalI abul

bsaJI BtyI

*END DHFR

mbol/ndell[dam-] dpnI[dam+] Bau3AI

nlalII

styl ncol

dpnII(dam-) alwI[dam-] betYI/xhoII

dsal bsmFI

ppu10I

tru9I mseI

aluI fnu4HI **DBOFI**

1101 ATGCATTIT ATAAGACCAT GGGACTTITG CTGGCTTTAG ATCCCCTTGG CTTCGTTAGA ACGCAGCTAC AATTAATACA TAACCTTATG TATCATACA TACGTAAAAA TATTCTGGTA CCCTGAAAAC GACCGAAATC TAGGGGAACC GAAGCAATCT TGCGTCGATG TTAATTATGT ATTGGAATAC ATAGTATGTG asel/asnl/vspl bbvI cacel beaJI neil/avalil

avall .. 196nee

aBuI

BCLFI INVE

FIG. 48D

ecoRII

ecoRI taqI apoI claI/bsp106 bspDI{dam-1 AT CGATTGAATT iA GCTAACTTAA	scrFI mval fnu4HI ecoRII dsav bstNI bsoFI apyl[dcm+] hael bbvI acii haelII/pali TCTGGCGGTG GCCTGGTGCA AGACCCCAC	scrFI scrFI scrFI scrFI scoRII dsav bstNI bslI apyI[dcm+] haelII/palI ll sau96I ccoOl091/dralI iralI asuI scTAA GGCCTGGAA
dsav tagi apol bstNi bstNi apol apol apyl[dcm+] mnli clai/bspl06 cAGGTGTCCA CTCCCAGGTC CAACTGCACC TCGGTTCTAT CGATTGAATT GTCCACGT GAGGTCCTAA GCTAATTAATT GTCAACTTAA GCTAACTTAA GCTAACTTAA GCTAACTTAA GCTCACA GATGACTTAA GCTCACATAA GCTCACATAA GCTCACATAA GCTCAACTTAA GCTCACATAA		scrFI ncii mspi dsav cauli smal/pspAi bsali bsali bsali bsali bsali bsali bsali bsali bsali ccoll091/dcai itv. ccoll091/draii sau96i itv. ccoll091/draii sau96i itv. ccoll091/draii sau96i v R Q A P G K G L E
dsav bstNI apyl[dcm+] mnll cl bsaJl bsaJl be GAGGGTC CAACTGCACC TGGGTTCTA GAGGGTCCAG GTTGACGTG AGCCAGATN seq from pRK6G425VH: Cla-Avrll^	rmal mael bfal alul cAGAAGTTCA GCTAGTGCAG GTCTTCAAGT E V Q L V Q	sau96I avali as bsri bsri TATGCACTGG ATACGTGACC
bali TTTCTCTCCA CAGGTGTCCA (rmal hpml/gsul[dcm-] bfal bsrl csp61 frctagtage aactgcaact ggagtacatt cangarana	ple1 hinfl taq1 xhol paeR71 aval maeI11 aval maeIII xrGGGAAGA GCTCAGTGAT x S F S S H Y F G G F S S H Y
mmelii hphi scfi foki ggtgacacta tagataacat ccactttgcc T ccactgtgat atctattgta ggtgaaacgg A	rmal rsal rmal nael bpml/gsul[dcm-] bfal bfal alul alul atggrcatgt atcatcttt ftctagrac aactgcaact ggagracatt cagaagtca gctagracat faccagraca aactacata catcatcatc faccagraca aactacata catcatcatcatcata catcatcatcatcatat catcatcatcatcatcatcatcatcatcatcatcatcatc	hgiJII bsp1286 bmyl scrFI mval banII ecoRII dsaV dsaV bstNI bsaJI apyl[dcm+] cCCAGGGGC TCACTCCGTT TGTCCTGTGC AGCTTCTGGC CGGTCCCCG AGTGAGCAA ACAGGACAG TCGAAGACCG p G S L R L S C A A S G
dsav ta bstni apyl(dcm+1 mnli cla hphi scfi foki bsaji pspidoraccaccaccaccaccaccaccaccaccaccaccaccacc	nlaili atyi pflHi ncol daai bali fok baaji CCACCATGGG	hgiJII bsp1286 bsp1286 bsp1286 bsp1286 bsp11 ecori dsav bstNI bsaJI apyl[dcm+] l401 GCAGGGGC TCACTCCGTT CGGTCCCCG AGTGAGCAA 14 P G G S L R L

thal fundII/mvnI fundII/mvnI betUI sau96I asu1 GTTCAAGGG CGTTTCACTT TATCTCGCGA CAACTCCAAA AACACAGCA CAAGTTCCG GCAAAGTGAA ATAGAGCGCT GTTGAGGTTT TTGTGTCGTA F K G R F T L S R D N S K N T A Y	hinli/acyl ahail/bahi bsri aatii maelii taqi hphi mboli maeli cchaggg attatccta caatggac tcctcttc acctctggg	sau961 sau961 lala1V lala2V lala2V
thai sau3Ai mbol/ndeIl[dam-] dpnI[dam+] dpnI[dam+] alwI[dam-] alwI[dam-] alwI[dam-] bsaAi 1501 TGGGTTGGAT ATATTGATGC TATCCAAAA TATATCAAAA AACAAGCAT ACCCAACCTA TATAACTACA CATTGATGC TATTAGTTTT CAAGTTCCG GCAAGTGAA ATAGAGGGTT TTGTGTGTTA TATGATTACAAGG AAGGTTACA TATTAGTTTT CAAGTTCCG GCAAGTGAA ATAGAGGGTT TTGTGTCGTA A7 W V G Y I D P S N G E T T X N Q K F K G R F T L S R D N S K N T A X	befi beti cac8! mnli bepMi bepMi l601 ACCTGCAGAT GAACAGCTG CGTCTGCCGT CTATTACTGT GCAACAGGGG ATTATCGCTA CAATGGTGA TGGTTCTTTCG ACGTCTGGGG TGGACGTCTA CTTGTCGGAC GCACGACTC TGTGACGCCA GATAATGACACT GTTACCACTG ACCAAGAAGC TGCACACCCC TGGACGTCTA CTTGTCGGAC GCACGACTC TGTGACGCA GATAATGACACT GTTACCACTG ACCAAGAAAGC TGCACACCCC TGGACGTCTA CTTGTCGGAC GCACGACTC TATAATGACA GTTACCACTG ACCAAGAAAGC TGCACACCCC TGGACGTCTA GTTACCACTG ACCAAGAAAGC TGCACACCCCC TGGACGTCTA CTTACCACTG ACCAAGAAAGC TGCACACCCCC TGGACGTCTA GTTACCACTG ACCAAGAAAGC TGCACACCCCC TGGACGTCTA TATAACAACTTC TGTACAACAACAACAAAAAACAAAAAAAAAA	sau961 nla1V nla1V bsp1201 mval bsm1286 ban1 mval bsm1201 mval bs

hinpi nari hgial/aspHI bspl286 kasi beiHKAI mspI hdici cac81 hpali hacii fnu4HI scrFI banl bsoFI ncii ahall/bsaHI acii apaLi/snoi dsav ddel hhal/cfoi nspBII alw44/snoi cauli GAACTCAGGC GCCCTGACCA GCGCGTGCA CACCTTCCCG CGTGTCCTAC CTTGAGTCCC CGCCACTGC CGCACGCTCAC N S G A L T S G V H T F P A V L Q	#HI hgici bani alul bsp1286 AGCTTGGGCA CCCAGACCTA CATCTGCAAC GTGAATCACA AGCCCAGCAA TCGAACCCGT GGGTCTGGT GTAGACGTTG CACTTAGTGT TCGGTCGTT S L G T Q T Y I C N V N H K P S N	BecrFI mval mval mval ecoRII dsav bstNI n] bstNI n] bmyl alwN[dcm-] apyI[dcm-] GTGCCCAGCA CCTGAACTCC TGGGG CACGGGTCGT GGACTTGAGG ACCCCC C P A P E L L G C
BCTFI mval ecoRII ecoNI daav bbsli bbli apy1[dcm+] bbli bbvI 1801 CTGGGCTGCC TGGTCAAGGA CTACTTCCCC GAACCGGTGA GGGACGACGA GACCGAACGACACT GCCACAGCACC GACCCGACGG CTGGCCACT GCCACAGCACC GACCCGACGC CTGGCCACT GCCACAGCACCACCACCACCACCACCACCACCACCACCAC	ddel plel fnu4HI bsoFI nlaIV aco811 mnl1 bbvI maeIII bfal aluI bsp1286 bsu361/mstII/saul ddel hphI bmyI mnl1 bbvI bmyI 1901 AGTCCTCAGG ACTCTACTCC CTCAGCAGCTGT GCCTCTAGC ACCTTGGGCT GCTTGGGCT TGAGAGCG TGAGAGAGCG TGAGAGAGCG TGAGAGAGCG TGAGAGAGC TGAGAGAGAG TA Y T V P S S L G T Y	hgijii nlaili bep1286 beaji bmyi maelli nspli banli sanli nspli banli maelli nspli scraacere carecerare treaceceare raterese ratereses carecerace cretretre arcrecett tagacecace greetrese cretretres arcrecett tagacecace greetrese cretretres arcrecett tagacettes and the second statement of the s

FIG. 48H

A K

/6aul 3T 2A F	En et	l baoFI bbvI 3G
mboli ddel bpuAl eco811 bb81 b8u361/m\$tII/sauI GAAGACCCT GAGGTCAAGT CTTCTGGGA CTCCAGTTCA	hphi hgal mnli GTGGTCAGCG TCCTCACCG CACCAGTCGC AGGAGTGGCJ V V S V L T V	fnu4HI b CCAAAGGG GGTTCCC
mboli ddei bpuAl eco811 bbsi bsu361 GAAGACCT GA CTTCTGGGA CT	hgalm Scc Ac	AA AGG
mboli bpual bbal CGAAGAC GCTTCTC	GTGGTCA CACCAGTCA V V S	CATCTCC
maeli ACGTGAGCCA TGCACTCGGT V S H	rsal cap6I maell baaal CACGTACCGT GTGCATGCCA	tagI TCGAGAAAA C AGCTCTTTT G
I GTGGTGGTGG CACCACCACC V V V D	real cap61 AGTACAACAG TCATGTTGTC Y N S	CCAGCCCC A
mboli del del mall denil[dam-] eco811 maelli beal/ksp6321 bsaJI mall bpuRi eco811 bsuJE1/ksp6321 bsaJI msli bspHI[dam-] asul bsuJ61/mstII/saul maell bsuJ61/mstII/saul bsuJ61/mstII/saul bsuJ61/mstII/saul bsuJ61/mstII/saul bsuJ61/mstII/saul psuJ61/mstII/saul crctrccccc carcacctc argarctccc ggacccttga ggrcacatcc grgtggrgg acgrgacca cgaagacct gaggrcaacatca argarcaacatca carcacacatca argarcaacatca argarcaacatc	Thai thai thai thai thai thai thai fuuDil/mvni bstui bstui bstui bstui bstui bstui bstui bstui bstui bsui real acii tuutii mnli real macii bsoFi bseli bsali hgai mnli TATTACGCTA GACAAAGCC GGGAGGAGC AGTACAACAG CACGTACCG GCGTCCCGC AGAGTGCCA AGAGTGCCCA AGAGTGCCCA AGAGTGCCCA AGAGTGCCCA AGAGTGCCCA AGAGTGCCCA AGAGTGCCCA AGAGTGCCCA AGAGTGCCA AGAGTACA AGAGTACA AGAGTA AGAG	econi batni
am-) eco8 asul bau3 c GGACCCTG G CCTGGGGAC R T P E	acilithar thar fundi batur batur sacil/ sacil/ sacil daai baaji acil fuutHI bachadccc cc	bemai baai AAGGTCTCCA TTCCAGAGGT K V S N
mnli dpnil(dam-) msli bspHI(dam-) asul cAcccrc ArgArcrccc GGAC GTGGGAG TACTAGAGGG CCTG T L M I S R T	ATAATGCCAA TATTACGGTT N A K	raal capéi GTACAAGTGC CATGTTCACG Y K C
I mell be JI mell be A GGACACCTC T CCTGTGGGAG D T L	maeII rsaI csp6I bsrI bsaAI 2201 TCAACTGGTA CGTGGACGTC AGTTGACCAT GCACCTGCG CACCTCCACG 281 N W Y V D G V E V H scrFI mvaI	ATGGCAAGGA TACCGTTCCT G K E
earl/kap6321 baaJI 101 CTCTTCCCCC CANAACCCAA GAGAAGGGGG GTTTTGGGTT (247 L F P R R P K	maeII al al p6I 8aAI A CGTGGACGC T GCACCTGCCG V D G	[bsr] [dcm+] GACTGGCTGA CTGACCGACT D W L N
earl/kap6321 1 CTCTTCCCC CAGAGGGGG G7 1 L F P P	mael raal csp61 bsrI bsaAI TCAACTGGTA CG AGTTGACCAT GC AGTTGACCAT GC	ecoNI batNI barI ball apyl[dcm+] CCTGCACCAG GACTG GGACGTGCTC CTGAC
210	2201	314

mboll ddel drdI

nlaIII

IHdau ldgu

> mnlI ddeI

mbol/ndell[dam-]

Cauli

nlaIII

Bau3AI avaII

dsav ncil

Bau96I nlaiv

hpall

MspI BCFF malI

styI bsaJI

Iloqu

rcal dpn1[dam+]

2401 CAGCCCCGAG AACCACAGGT GTACACCCTG CCCCCATCCC GGGNAGAGAT GACCAAGAAC CAGGTCAGCC TGACCTGCCT GGTCAAAGGC TTCTATCCCA GICGGGGCIC TIGGIGICCA CAIGIGGGAC GGGGGIAGGG CCCTICICIA CIGGITCTIG GICCAGICGG ACTGGACGGA CCAGITICCG AAGAIAGGI TOLVKG apyI[dcm+] **betNI** mval bapMI ecoRII apyI[dcm+] ecoRII **b**etNI 4887 BexAI mvaľ bspl4071/bsrGI bslI aval earl/ksp6321 ball bead mboll SCLFI Cauli dsav nctI fokI сврбІ

BCLFI

xmal/pspAI

BmaI

caull hpaII

BCLFI

ncil Idem dsaV 7 S A O

z ×

E E

P P S R

7 1

У

347 Q P R E

MapI

nlalv mboli scfi cac8] 2501 GCGACATEGE CGTGGAGTGG GAGAGCAATG GGCAGEEGGA GAACAACTAE AAGAECAEGE ETEECGTGET GGACTECGAE GGCTECTTET TECTETACAG CGCTGIAGCG GCACCTCACC CICICGITAC CCGTCGCCT CITGITGATG TICIGGTGCG GAGGGCACGA CCTGAGGCTG CCGAGGAAGA AGGAGATGITC
D I A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S mnlI hinfi pleI mnlI hpall fnu4HI baoFI bbvI berDI mell beaJI dsal bell

earI/kso632I 2601 CAAGCTCACC GTGGACAAGA GCAGGTGGCA GCAGGGGAAC GTCTTCTCAT GCTCGTGAT GCATGAGGCT CTGCACAACC ACTACACGCA GAAGAGCTTC GITCGAGIGG CACCIGITCI CGICCACCGI CGICCCCIIG CAGAAGAGIA CGAGGCACIA CGIACICCGA GACGIGITGG IGAIGIGCGI CIICICGGAG mboll mull Bapl Y G HNHI H E mnll nsil/avallI nlallI BfaNI S < nlaIII VFSC bpuAI xmnI bbsI maeII asp700 fnu4HI **DBOFI** Lvdd IMqad Z Z VDKS alul bsaJI deal hphI 414 K L T

Ilodm

FIG. 48I

maelii Aatggtaca ttaccaatgt	nlaiii alwi[dam-] ATCATGTCTG TAGTACAGAC
aluI fnu4HI bsoFI bbvI TGCAGCTTAT	AATGTATCTT TTACATAGAA
fnu4HI aBuI bsoFI nlaIII sf11 styl eae! nco! cfr! dsa! alul haeIII/PalI hindIII bgl! bsaJI in AGCTTGGCC CCATGGCCC ACTTGTTTAT:	rmal mael bfal ctagtt gtggtttgtc caaactcatc gatcaa caccaaacag gtttgagtag
tagi plei rmai sali sefi maei hincil/hindii e sau96i hinfi psti haeili/pali bsgi alui sgu cccragagt Gaccragagt cc ggarcrcag Gaccragagt wo:71)	rmal mael bsml bfal bfal ATAAAGCATT TTTTTCACTG CATTCTAGT TATTCGTAA AAAAAGTGAC GTAAGATCA
taqI fin4HI asuI haliI haliI asuI pleI tmai sali sfil styl styl sau96 hincil/hindil eael ncol dsav haeIII/pall bsgl alul haeIII/pall bsgl alul haeIII/pall bsuJ bsmAI asuI bfaI acci bspMI hindili bgli bsaJI bbvI harGCTACA ACTTGTTAT TGCAGCTTAT AATGGTTACA AGGACAAGA GCCATGACGC GCATGACGC GCTACACGC GCTACCAATGT TAACCAATGT TAACAAATA ACTCGAATA TTACCAATGT AGGACAAGA GCCATTAAC TCACGATCTAA GCTGAACATAT TCAACAATAT TAACCAATGT AGGACAATAT TAACCAATGT TAACAAATA ACTCGAATA TTACCAATGT AGGACAAGA GCCATTAAC TCAACAATAT ACCAATGT TAACAAATA ACTCGAATA TTACCAATGT AGGACAAGA GCCATTAACAAATA ACTCGAATAA ACTCGAATA TTACCAATGT AGGACAAGA GCCATTAACAAAATA ACTCGAATA TTACCAATGT AGGACAAGA GCCATTAACAAAATA ACTCGAATAA ACTCGAATAA ACTCGAATAA ACTACAAAATA ACTCGAATAA ACTACAAAATA ACTACAAAATA ACTACAAAATA ACTACAAAATA ACTACAAAATA ACTACAAAATA ACTACAAAATA ACTACAAAATA ACTACAAAAAAAA	rmal mael bemi bfal 2801 AATAAAGCAA TAGCATCACA AATTICACAA ATAAAGCATT TTTTTCACTG CATTCTAGTT GTGGTTTGTC CAAACTCATC AATGTATCTT ATCATGTCTG TTATTTCGTT ATCGTAGTGT TTAAAGTGTT TATTTCGTAA AAAAAGTGAC GTAAGATCAA CACCAAACAG GTTTGAGTAG TTACATAGAA TAGTACAGAC

haeIII/palI

sau96I

dpni[dam+] asp710 hhal/cfol nlaili mnli acc651 ddel acii dpni[dam-] asel/asni/vspi bsaJi mnli mnli acc551 ddel acii 2901 GATCGATCGG GAATTAATTC GGCGCAGCAC CATGGCTGA AATAACCTCT GAAAGAGAA CTTGGTTAGG TACCTTCTGA GGCGGAAAGA ACCATCTGTG CTAGCTAGCC CTTAATTAAG CCGCGTCGTG GTACCGGACT TTATTGGAGA CTTTCTCCTT GAACCAATCC ATGGAAGACT CCGCCTTTCT TGGTAGACAC csp6I hgici rsal nlaIV banI kpnI dsal haelll/pall hael bsoFI styI bbvI ncoI fnu4HI hinPI mbol/ndell[dam-] tagl[dam-] tru9I bspDI[dam-] mseI clai/bsp106[dam-] mbol/ndell[dam-] Icmx dpnII(dam-) dpnI[dam+] pvul/bapCI sau3AI. **be1EI** mcrI Bau3AI

FIG. 48J

ppul0I ppul0I ppul0I nlaIII sphI sphI sphI sphI sphI sphI sphI s	acii bemfi acii foki GTCAGCAACC ATAGTCCGC CCCTAACTCC GCCCATCCCG CCCCTAACTC CAGTCGTTGG TATCAGGCG GGGATTGAGG CGGGTAGGGC GGGGATTGAG	ali I ddel JI mnli alui mnli haeili/pali TCGGCCTCT GAGCTATTCC AGAAGTAGTG
BfaNI PpulOI PpulOI nlaIII BphI nsplI nspHI cacli CTTCATACGT TTCGTACGTA G	acii bemfi stcagcaacc atagtcccgc c	fnu4HI bsoFI bsJI sf11 haelII/palI mnlI mnlI dde] mnlI bsaJI acil haelII/pe FATGCAGAGG CCGAGGCCGC CTCGGCCTCT (ATACGTCTC GGCTCCGGCG GAGCCGGAGA (ATACGTCTC GGCTCCGGCG GAGCCGGAGA (ATACGTCTC GGCTCCGGCG GAGCCGGAGA (ATACGTCTC GGCTCTCGGCG GAGCCGGAGA (ATACGTCTC GGCTCCGGCG GAGCCGGAGA (ATACGTCTC GGCTCTCGGCG GAGCCGGAGA (ATACGTCTC GGCTCCGGCG GAGCCGGAGA (ATACGTCTC GGCTCTCGGCG GAGCCGGAGA (ATACGTCTCC GGCTCTCGGCG GAGCCGGAGA (ATACGTCTCC GGCTCTCGGCG GAGCCGGAGA (ATACGTCTCC GGCTCCGGCG GAGCCGGAGA (ATACGTCTCC GGCTCTCGGCG GAGCCGGAGA (ATACGTCTCC GGCTCTCGGCG GAGCCGGAGA (ATACGTCTCC GGCTCTCGGCGCGGCGGGGGGCGGGGGGGGGG
BCLFI	nlalv scri scri mval ecoRII dsav bstNI bstNI apyl[dcm+] bsaJI cac8I 3101 TCCCCAGGCT CCCAGCAGC CACAACTATC ATCTCAATTA GTCAGCAACC ATAGTCCGC GCCTAACTC AGGGTCGA GGGTCGTCC GTCTTCATAC GTTTCGTAC TAAACTAAT CAGTCGTTGG TATCAGGCC GGGGTTGAGG CGGGTAACTC scrib apyl[dcm+] acil bsaJI acil bsaJI acil bsaJI cac8I 3101 TCCCCAGGCT CCCCAGCAGC CCCTAACTC AGGGTCGTCG GGGTTAAT CAGTCGTTAAT CAGTCGTTGG TATCAGGCC GGGGATTGAG AGGGTCCGA GGGTCGTCC GTCTTCATAC GTTTCGTAC TAAACTTAAT CAGTCGTTGG TATCAGGCC GGGGTTAACC AGGGTCCGA GGGTTAAC GTTTCGTAAC TAAACTTAAT CAGTCGTTGG TATCAGGCC GGGGTTAACC AGGGTCCGA GGGTTCATAC GTTTCGTAAC TAAACTTAAT CAGTCGTTGG TATCAGGCC GGGGTTAACC AGGGTCCGA GGGTTAAC GTTTCGTAAC TAAACTTAAT CAGTCGTTGG TATCAGGCC GGGGTTAACC AGGGTCCGA GGGTTAAC GTTTCATAAC GTTTCATAAT CAGTCGTTGG TATCAGGCC GGGGTTAACCC AGGGTCCGA GGGTTAAC GTTTCATAAC GTTTCATAAT CAGTCGTTGG TATCAGGCC GGGGTTAACCC AGGGTTCGA GGGTTCATAAC GTTTCATAAT CAGTCGTTGG TATCAGGCC GGGGTTAACCC AGGGTTCGA GGGTTAACC ATAGTCCCAAACTTAAC TAAACTTCAAACTTCAAACTTCAAACTTAAC GTTTCATAAT CAGTCGTTGG TAACAGCAACCCAAACTTAAACTTCAAACTTAAACTTAAACTTCAAAACTTAAACTTCAAACTTAAACTTCAAACTTAAACTTCAAACTTAAACTTCAAACTTAAACTTCAAACTTAAACTTCAAACTTAAACTTAAAACTTCAAAACTTAAAACTTCAAAACTTAAAACTTAAAACTTAAAACTTCAAAACTTAAAACTTAAAAACTTAAAAAA	fnu4HI bBOFI bglI stil ncol bslI dsal bslI dsal acil bsali 3201 CGCCCAGTTC CGCCCATG CCACTGATTA TTTTTTTATT TATGCAGAGG CGGGGGGGGGG

FIG. 48K

tfil hinfi acii thai fnuDiI/mvni bstUI bsh1236i cGCGGATTCC CCGTGCCAAG AGTCAGGTAA GCGCCTAAGG GCCACGGTTC TCAGTCCATT U1 matched splice donar^	sau3AI mbol/ndeII[dam-] dpnI[dam+] dpnII[dam-] taqI[dam-] clal/bspl06[dam-] bspDI[dam-] sau3AI mbol/ndeII[dam-] dpnII[dam-] trG GAAACCTACTG ACACTGACAT TrG GAAAACCTAG CTAGGATGAC 'removed ATG 'removed ATG 'lariat consensus' IgG vH natural lariat restored'
scrFI ncii mcii hpail deav haelil/pali ul mcri eagl/xmaili/eclXi eaci cfri bsiEi mspi cauli hpail GCTTATCCG CCGGGAACGG TGCATTGGAA Avrii - Hindili frag	fnu4HI bsoFI acil thai thai thai haelII/pali asul bsaJi AGGCCCACCC CCTTGGCTTC GTTAGAACGC GGCTACAATT AATACATAAC TCCGGGTGGG GGAACCGAAG CAATCTTGCG ASDE AGGCCACCC CCTTGGTTC ATAGAACGT AGGCCAACTTGCT AGGCCAACTTGCG TAGGAACGAAGTTAA TTATGTATTGTAT
scrFI rmal mael styl styl baaJI baaJI cagl/xmall/el avrII[dam-] haelII/pall haelII/pall haelII/pall haelII/pall haelII/pall haelII/pall stul nhel hael haelII/pall haelII/pall haelII/pall avrII[dam-] haelII/pall haelII/pall haelII/pall cagl/xmalII/el haelII/pall ha	acil Bcfi cspi blei cspi scfi hinfi GTACCGCCTA TAGAGTCTAT CATGGCGGAT ATCTCAGATA
3301	3401

FIG. 48L

nlalli etyl pflMi ncol dsel sRi dsel sI bell fokl drrc caccargga	mplI acti	
clal/bsp106 pf] sfaNI ecoRI fnu4HI ecoRI bbor bspDI[dam-] r GGCTGCATC GATTGAATTW	I I I I I I I I I I I I I I I I I I I	ATGACCGAGT CCCCAACAC CAACAGGGGGGGGGGGGGG
rmal mael bfal thal nhel fnuDII/mvnI bstUI cac8I bstUI cac8I cc TCGGTTCGCG AAGCTAGCT' GG AGCCAAGCGC TTCGATCGA		AGATATCCAG TCTATAGGTC D I Q EnaBI BRAAI GGTGCTAGGT CCACGATGCA G A T X
sau961 avaii asui mael mael mvai ecoRii thai nhei sfaNi daav batNi batUi cac8i fnu4Hi ecoRi apyi[dcm+] mnli bsh1236i alui bspin[dam-] crcccAGGTC CAACTGCAC TCGGTTCGC AACTACATC GAGGTCCAG GTTGACGTG AGCTAAGTAAG classic caactaa caactaag	real bpml/gaul[dcm-] berl cep61	ACTGCAACTG GAGTACATTC TGACGTTGAC CTCATGTAAG ALUI CBP6I hindIII nlaIII AAAGCTTAGT ACATGGTATA TTTCGAATCA TGTACCATAT S L V H G I S L V H G I
bell caggreer	rmal mael foki bfal	GAAAA AGATCATGGT BCI BCI BBJI BBBJB7I BBPMI AL BBPMI ACTGC AGGTCAAGTC CGGACG TCCAGTTCAG CCTCC AGGTCAAGTC CGGACG TCCAGTTCAG CCTCC AGGTCAAGTC CGGACG TCCAGTTCAG CCTCC R S 9 Q
3501 CCACTTTTC TTTTCTCCA GGTGAAAAG AAAAAGAGT	e in the interval of the inter	57

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fnu4HI
                                                                        bsoFI
                                                                                         PpvI
                                                                                                                                                                                                                                                                                                                                                                    haeIII/palI
                                                                                                     BcfI
                                                                                                                   pstI
                                                                                                                                  bagi
                                                                                                                                                                                                                                                            mbol/ndell[dam-] fnu4HI
                                                                                     3801 ACTACTGATT TACAAAGTAT CCAATCGATT CTCTGGAGTC CCTTCTGGATC CGGTTCTGGG ACGGATTTCA CTCTGACCAT CAGCAGTCTG
                                                                                                     TGATGACTAA ATGTTTCATA GGTTAGCTAA GAGACCTCAG GGAAGAGCGA AGAGACCTAG GCCAAGACCC TGCCTAAAGT GAGACTGGTA GTCGTCAGAC
                                                                                                                                                                                                                                                                                    bsoFI
                                                                                                                                                                                                                                                       3901 CAGCCAGAAG ACTTCGCAAC TTATTACTGT TCACAGAGTA CTCATGTCCC GCTCACGTTT GGACAGGGTA CCAAGGTGGA GATCAAACGA ACTGTGGCTG
                                                                                                                                                                                                                                                                        GTCGGTCTTC TGAAGCGTTG AATAATGACA AGTGTCTCAT GAGTACAGGG CGAGTGCAAA CCTGTCCCAT GGTTCCACCT CTAGTTTGCT TGACACCGAC
                                                                                                                                                                                                                                                                                                                                      TVAA
                                                                                                                                                                                                                                                                                                                                                     4001 CACCATCTGT CTTCATCTTC CCGCCATCTG ATGAGCAGTT GAAATCTGGA ACTGCTTCTG TTGTGTGCCT GCTGATAAC TTCTATCCCA GAGAGCCAA
GTGGTAGACA GAAGTAGAAG GGCGGTAGAC TACTCGTCAA CTTTAGACCT TGACGAAGAC AACACGGA CGACTTATTG AAGATAGGGT CTCTCCGGTT
                                                                                                                                                                      လ
                                                                                                                                                                 LTI
                                                                                                                                                                                                                                                                                                                                  IKR
                                                                                                                                                                                                                                                  Bau3AI
                                                                                                                                                        T D F T
                                                                                                                                                                                                                                                                                                                             X <
                                                                                                                                                                                                                                                     banl baall
                                                                                                                                                                                                                           kpnI styI
         mbol/ndell[dam-]
                                                                                                                                                                                                    Cep6I
                                                                                                                                                                                                                nlaiv
                                                                                                                                                                                     rsal
                                                                                                                                                                                                                                           haici
                                       dpnII[dam-]
                       dpnI{dam+}
                                                   alwi[dam-]
                                                                             batYI/xhoII
Sau3AI
                                                                   nlaiv
                                                                                                                                                                                                                                              acii
                                                                bpmI/gauI[dcm-]
                                                       DSmFI
                                                                        clai/bsp106 pleI
                                                 hinfi
                                      tfil
                                                                tagi
                                                                                                                                                                                                                                                                                                                                                    mboll acil
                                                                                                                                                                                                                                                                                                                                    DPuAI
                                                                                                                                                                                                                                                                                                                                                   ppeI
                                                                                                                                                                                                                                        bpuAI
                                                                                                                                                                                                                                                    ppeI
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hpall beawi

MepI psll ۲ م

F

FIG. 48N

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4101 AGTACAGTGG AAGGTGGATA ACGCCTCCA ATCGGGTAAC TCCCAGGAGA GTGTCACAGA GCAGGACAGC AAGGACAGCA CCTACAGGCT CAGCAGCACC
                                                      4201 CTGACGCTGA GCAAAGCAGA CTACGAGAAA CACAAAGTCT ACGCCTGCGA AGTCACCCAT CAGGGCCTGA GCTCGCCCGT CACAAAGAGC TTCAACAGGG
                                                                                                                                                                                                                                                                          GACTGCGACT CGTTTCGICT GAGGTTTCAGA TGCGGACGCT TCAGTGGGTA GTCCCGGACT CGAGCGGGCA GTGTTTCTCG AAGTTGTCCC
                                                                                                                                                                                                                                                                                                                                                                                                                   4301 GAGAGTGTTA AGCTTGGCC CCATGCCCCA ACTTGTTTAT TGCAGCTTAT AATGGTTACA AATAAAGCAA TAGCATCACAAT TCGAACCGGC GGTACCGGGT TGAACAAATA ACGTCGAATGT TTATTTGGTT ATCGTAGTGT TTAAAGTGTT TATTTCGTT ATCGTAGTGT TTAAAGTGTT TATTTCGTA
                                                                                                                 YSL
                                                                                                                                                                    hgiAI/aspHI
                                                                                                                                                                                 ecl136II
                                                                                                                                                                                                                              ddel cac81
                                                                                                                                                                                               bsp1286
                                                                                                                                                                                                         DEIHKAI
                                                                                                                                                           hgiJII
                                                                                                                                                                                                                                         haeIII/palI
                                                                                                                                  sstI
                                                                                                                                                Baci
                                                                                                                                                                                                                      bmyI
                                                                                                                                                                                                                                                     Bau96I aluI
             CCORII
                                  batnI
MVal
                       dsav
                                                                                                                                                                                                                                                                                                                                                                                                    aluī
                                                                                                                                                                                                                                                                                                                                                                                                             fnu4HI
                                                                                                                                                                                                                                                                                                                                       haeIII/palI
                                   mnll
                                                                                                                                                                                                                                                                                                                                                      Inep
                                                                                                                                                                                                                                                                                                                                                          bsoFI nlaIII
                                                                                                                                                                                                                                                                                                                                                                             aluI haeIII/palI
                                                                                                                                                                                                                                                                                                                                                                     Bfil Btyl
                                                                                                                                                                                                                                                                                                                                                                                          hindili bgli ncol
                                                                                                                                                                                                                                                                                                                                                                                                              deal
                                                                                                                                                                                                                                                                                                                                                 fnu4HI
                                                                                                                                                                                                                                            blpI/bpull021
                                                                                                                                                                                                                                                                                                                                                                                                    tru91 eael
                                                                                                                                                                                                                                 cellI/espl
                                      Cep61
                          real
                                                                                                                                                                                                                                                         hqaI
```

SCLFI

FIG. 480

Eau3AI mbol/ndcI[dam-] dpnI[dam-] dpnI[dam-] pvul/bspCI mcrl bsiEI taqI[dam-] claI/bspCI bsiEI taqI[dam-] claI/bspCI bsiEI taqI[dam-] claI/bspCI bsiEI taqI[dam-] bsiEI taqI[dam-] bsiEI taqI[dam-] bsiEI taqI[dam-] bsiEI bsiAI bsiAI dpnI[dam-] dpnI[dam-] aseI/asnI/vspI bsiAI intell dpnI[dam-] aseI/asnI/vspI bsiAI intell dpnI[dam-] aseI/asnI/vspI bsiAI intell briAI csiCCCTCCTC ccCTAAATTAATTC csiCCACCCTC ccCTAAATTAATTC csiAI csiAI csiAI csiAI csiAI csiAI csiACCCCTCAA craccacc craccacc craccacc craccacc craccacc craccaccacc craccaccaccacc craccaccacc craccaccaccacc craccaccaccacc craccaccaccacc craccaccaccaccacc craccaccaccaccaccaccacc craccaccaccaccaccaccaccaccaccaccaccaccac	GGAA CTTGGTTAGG TACCTTCTG AGGGGAAAGA ACAGGTGTG GAATGTGTG CAGTTAGGGT GTGGAAAGT CCAGGCTGC GAATGTGTGT CAGTTAGGGT GTGGAAAGT CCAGGCTGT GAATGTGTGT CAGTTAGGGT GTGGAAAGTC CCAGGGTCC ATGGAAAGTC TGGTCGACAC CTTACACACA GTCAATCCA CAGGAAAGTC CCCAGGGTCC AAAAAAAAAA	Prototol nationalists nationalists sphi sphi napi napi napi napi napi napi Tregracera creaters Fig. 48P
rmal maei bsmi bfai 4401 TITITCACTG CATICTAGIT GTGGTITGTC AAAAAGTGAC GTAAGATCAA CACCAAACAG	mnli mnli TATTGGAGA CTTTCTCCTT GAACCAAT	PPULO PPULO 10 11 1 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1

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aPyI[dcm+]
                                                                                                                                                                                 MaeIII
        ecoRII
                                                                                                                                                                                                                                                                                               BCLFI
                                                                                                                                                                                                                                                                                                                                      betNI
                                                                                                                                                    ABADANTATT TATGCAGAGG CCGAGGCCGC CTCGGCCTCT GAGCTATTCC AGAAGTAGTG AGGAGGCTTT TTTGGAGGC TAGGCTTTTG CAAAAAGTG
AAAAAATAA ATACGTCTCC GGCTCCGGCG GAGCCGGAGA CTCGATAAGG TCTTCATCAC TCCTCCGAAA AAACCTCCGG ATCCGAAAAC GTTTTCGAC
                                                                                                                                                                                                                                                                                                                             dsav
                                                                                                                                                                                                                                                                                                         MVaI
                                                                                                                                                                                                                                                                                                                                                          beaJI
                                                                                                                                                                                                                                                                                                                    ANTGGAGCTC GCCGCCAAT TAATTCCGCG CGCATTTAAA TCCTGCAGGT AACAGCTTGG CACTGGCGGT CGTTTTACAA GGTCGTGACT GGGAAAACCC
                                                                                                                                                                                                                start pucile.
nlalii
                                                                                                                                      avrII[dam-]
                                                                                                                                               haeIII/palI
                                                                                                 MaeI
                                                                                                                   bsaJI
                                                                                       rmaI
                                                                                                                              blnI
                                                                                                          styl
                                                                                                                                                                                                                                                                                                            haeIII/pall
                                                                                                                                                                                                                                                                                JRdsq
                                                                                                                                           haeIII/pali bsaJi mnli alui
                                                                                                                                                                                                                                                                                                      pstI
                                                                                                                                                                                                                                                                                            scfI
                                                                                                                                                                                                                                                                                                          ahalii/drai
                                                                                                                                                                                                                                                                                                  tru91
                                                                                                                                                                                                                                                                                                            meel trus: bah1236I msel
                                                                                                                                                                                                                                                     fuuDII/mvnI
                                                                                                                                                                                                                                 hhaI/cfoI
                                                                                                                           haeIII/pall
                                                                                                                                                                                                                                                                                  hhaI/cfoI
                                                                                                                                        mnll
                                                                                                                                                                                                                       hinpi
                                                                                   fnu4HI
    acil
                                                                                                                                                                                                                                                               bstur
                                                                                             bsoFI
                                                                                                                                                                                                                                                                                              Cac8I
                                                                                                                                                                                                                                   eagl/xmall1/eclXI thal
                                                                                                        pq1I
                                                                                                                                                                                                                                                                         hinpi
                                                                                                                  sfil
                                                                                                                                                                                                                                                                                                        ascI
                                                                                                                                      mnll
                                                                                                                                                                                                               haelli/pall
                                                                                                                                                                                                                                                                                          tru91
                                                                                                                                                                                                                                                                                             paeR71 bsiEI pacI
                                                                                                                                                                                                                                                                barBI baoFI
                                                                                                                                                                                                                                                eael
                                                                                                                                                                                                                                                                                   xhoI fnu4HI
                                                                                                                                                                                                                                                                             cfrI
                                                                                                                                                                                                                                                                                                          aval baoFI
                                                                                                                                                                                                                                                          notI
                                                                                                                                                                                                                                                                            tagi
```

FIG. 48Q

saug61 mbol/ndeII[dam-] haeIII/palI dpnI[dam+] asul dpnI[dam+] mnl1 acil pvul/bspcI earl/ksp6321 bsiEI GAAGAGGCC CGCACCGATC GCCTT	TCCGG GCGTGGCTAG CGGGAAGGT TGTCAACGCA	thal thal thal thal fluudil/mvnI bstUI scfI bstUI scfI bsh12361 GTGCGGTATT TCACACCGCA TACGTCAAAG CAACCATAGT ACGCGCCTG CACGCCATAA AGTGTGGCGT ATGCAGTTTC GTTGGTATCA TGCGCGCGC	hinpi hhal/cfoi hinpi haeii hhal/cfoi bsrBi aeiimaei acii bfai cacBi 3CGCCCTA GCGCCCGCTC CTTTCGCTTT CTTCCCTTCC
cac81 mbol/ndeIl[dam-] maeIII tru9I bsoFI pvuII mseI pvuII mbolI cac8I mbolI cac8I dpnI[dam-] TGGGTTACC CACTTAATC GCCTTGCAGC ACATCCCCC TTCGCCAATGG GTTCAATTAG CGAACGTCG TGTAGGGGG AAGCGTCGA CCCATTAATC CGACCGATC GCCTTAATC CAACGTCG TGTAGGGGG AAGCGGTCGAATTAG CGAACGATC GCCTTTAATC CAAACAGGCC CGCAACGATC GCCTTTAATC CAAACAGGCC CGCACCGATC GCCTTAATAC CGAACGATC GCCTTAATAC CGAACAGATC GCCTTAATAC CGAACACTCTAATAC CGAACACACATCAATAC CGAACACACAATCAATAC CGAACACACAATCAATAC CGAACACACAATCAATAC CGCAACACAATCAATAC CGAACACAATACAAT		Sfani Ataaaagagg aatgegtaga fnu4HI	bsoFI hinpI hinpI hhal/cfoI thaI fuuDII/mvnI bstUI bsh12361 acii h GGTTACGCG AGCGTGCCG CACCTCCC CACCTACCC CACCTACCC CACCTACCC CACCTACC CATGTGAACG GTC FIG ARB
tru91 maeIII mseI ACGCATTACC CAACTTAATC GCCTT	hinpi hhal/cfoi nlaiv nari kasi hini/acyi	efa Absahi SCTGAT SGACTA(thai fuuDII/mvnI hhai/cfoI hinpi fnu4HI hhai/cfoI bsoFI tru9I acli acli mseI bshl236I ATGGCGGGT TTAAGGGGG GGGTGTGGT

FIG. 48R

5301 TTTCTCGCCA CGTTCGCCGG CTTTCCCCGT CAAGCTCTAA ATCGGGGGT CCCTTTAGGG TTCCGATTTA GTGCTTTACG GCACTCGAC CCCAAAAAAC AAAGAGGGT GCAAGGGGC GAAAGGGGCA GTCGAGATT TAGCCCCCGA GGGAAATCCC AAGGCTAAAT CACGAAATGC CGTGGAGCTG GGGTTTTTTG 5401 TTGATTTGGG TGATGGTTCA CGTAGTGGGC CATCGCCCTG ATAGACGGTT TTTCGCCCTT TGACGTTGGA GTCCACGTTC TTAATAGTG GACTCTTGTT AACTAAACCC ACTACCAAGT GCATCACCCG GTAGCGGGAC TATCTGCCAA AAAGCGGGAA ACTGCAAACCT CAGGTGCAAG AAATATCAC CTGAGAACAA 5501 CCANNCTGGA ACNACACTCA ACCCTATCTC GGGCTATTCT TTGATTTAT AAGGGATTTT GCCGATTTCG GCCTATTGGT TAAAAAATGA GCTGATTTAA GGTTTGACCT TGTTGTGAGT TGGGATAGAG CCCGATAAGA AAACTAAATA TTCCCTAAAA CGGCTAAAGC CGGATAACCA ATTTTTACT CGACTAAATT 5601 CAAAAATTTA ACGCGAATTT TAACAAAATA TTAACGTTTA CAATTTTATG GTGCACTCTC AGTACAATCT GCTCTGATGC CGCATAGTTA AGCCAACTCC GITITIAAAT TGCGCTIAAA AITGIITIAT AATTGCAAAT GITAAAATAC CACGTGAGAG TCATGIIAGA CGAGACIACG GCGTAICAAT TCGGTTGAGG hgiAI/aspHI ddeI bsp1286 **bsilika**I Dm y I **bsp1286** nlaIv hglJII Psp14061 MaeII tru91 196nes cfr101/bsrFI apol tru91 hpall mseI Mspl fuuDII/mvnI naeI msel bstul hphI tru9I

tru91

5701 GCTATCGCTA CGTGACTGGG TCATGGCTGC GCCCCGACAC CCGCTGACGC GCCTGACGG GCTTGTCTGC TCCCGGCATC CGCTTACAGA CGATAGCGAT GCACTGACCC AGTACCGACG CGGGGTTGTG GGCGACTGCG CGGGACTGCC CGAACAGACG AGGCCGTAG GCGAATGTCT FIG. 48S

BfaNI

hpall BCLFI MBpI

funDII/mvnI hhaI/cfoI hinpi

bstur thaI

nlallI hhal/cfol

bsaAI tthllll/aspI bbvI

maell bari

MaellI

hinpi fnu4HI **b**80FI

```
hg1AI/aspHI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           apaLI/snoI
                                                                                                                       haelll/pall
                                                                                                                                                              eco01091/drall
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    bsp1286
                                                                                                      SB01 CAAGCTGTGA CCGTCTCCGG GACCTCATG TGTCACAGGT TTTCACCGTC ATCACCGAAA CGCGCGAGGC AGTATTCTTG AAGACGAAAG GGCCTCGTGA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  DB1HKAI
                                                                                                                          GTTCGACACT GGCAGAGGCC CTCGACGTAC ACAGTCTCCA AAAGTGGCAG TAGTGGCTTT GCGCGCTCCG TCATAAGAAC TTCTGCTTTC CCGGAGCACT
                                                                                                                                                                                                                                                                                            ATGCGGATAA ANATATCCAA TTACAGTACT ATTATTACCA AAGAATCTGC AGTCCACCGT GAAAAGCCCC TTTACACGCG CCTTGGGGAT AAACAAATAA
                                                                                                                                                                                                                                                                            5901 TACGCCTATT TTTATAGGTT ANTGTCATGA TAATAATGGT TTCTTAGACG TCAGGTGGCA CTTTTCGGGG AAATGTGCGC GGAACCCCTA TTTGTTTATT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        mbol/ndell[dam-]
                                                                                                                                                                                                                                                                                                                                                                                AAAGATTTAT GTAAGTTTAT TGTATCCGCT CATGAGACAA TAACCCTGAT AAATGCTTCA ATAATATTGA AAAAGGAAGA GTATCAGTAT TCAACATTTC
AAAGATTTAT GTAAGTTTAT ACATAGCCGA GTACTCTGTT ATTGGGACTA TTTACGAAGT TATTATAACT TTTTCCTTCT CATACTCATA AGTTGTAAG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      dpn1[dam+] bmy1
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             GCACAGCGCG ANTANGGGAN ANANGGCON TITIGCCTIC CIGITITIGG TONCCCAGAN ACGCTGGTGN ANGINANAGA IGCTGANGAT CAGITGGGTG

GCACAGCGGG ANTANGGGAN ANANGGCCGT ANANGGCANANANGG AGTGGGTCTI IGCGACCACT ITCATITICI ACGACTICIA GICANACCCAC
                                                                                                                                                                                                                                                              fnuDII/mvnI
                                                                                                                                                                                                                      nlaIv
                                                                                                                                                                                                                                    acti
                                                                                                                                                                                                                                                 thaI
                          funDII/mvnI
                                                       b8h1236I
                                                                                  hhal/cfol
                                                                                               thal mull
                                         betul
                                                                     hinpi
                                                                                                                                                                                                                                                                     ahall/bsaHI
                                                                                                                                                                                                                                                       hinli/acyi
                                                                                                                                                                                                                                                                                                                                                                              bsmAI
                                                             IHdgu
                                                                                                                                                                                                                                                         nlaIII
                                                Ideu
                                                                        fnu4HI
                                                                                                                                                                                                                                                                                                                                                                            berBI
                                                                                         bsoFI
                                                                                                                                                                                                                                                                          rcal
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            fnu4HI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          bBoFI
                                                                                                                                                                                                                                                                    tru91
BCLFI
                                          hpall
             ncil
                            MepI
                                                       daav
                                                                                         maelli bamAl
                                                                   esp31
                                                                                  DemBI
```

alw441/snol

FIG. 48T

GIGCICACCC AAIGIAGCII GACCIAGAGI IGICGCCAII CIAGGAACIC ICAAAAGCGG GGCIICTIGC AAAAGGIIAC IACICGIGAA AAITICAAGA 6201 CACGAGIGGG TIACAICGAA CIGGAICICA ACAGCGGIAA GAICCIIGAG AGIIIICGCC CCGAAGAACG IIIICCAAIG AIGAGCACII IIAAAGIICI ahallI/dral bsp1286 tru91 msel hqiAI/aspHI **DSIHKAI** bmyI psp1406I maell asp700 I CWX mbol I mbol/ndell[dam-] dpnII[dam-] alwI[dam-] dpnI[dam+] alwi[dam-] acii bstYI/xhoII sau3AI mbol/ndell[dam-] sau3AI nspBII berl dpnII[dam-] bstYI/xhoII dpnI[dam+] maeIII taqI

scal hphi maelli 6301 GCINTGIGGC GCGGIATIAI CCCGIGATGA CGCCGGGCAA GAGCAACICG GICGCCGCAI ACACIATICI CAGAATGACI IGGIIGAGIA CICACCAGIC csp61 bsrl ddeI fnu4HI begI belEI bsoFI mcrI ahall/bsallI hpall hinll/acyl hgal caull ncil Idsm dsaV fnuDII/mvnI **bsh1236I** hhal/cfol acil bstUI hinpi

BCLFI

Bau3AI CGATACACCG CGCCATAATA GGGCACTACT GCGGCCCGTT CTCGTTGAGC CAGCGGCGTA TGTGATAAGA GTCTTACTGA ACCAACTCAT GAGTGGTCAG

dpnII[dam-] dpn I [dam+] pvuI/bspCI **be1EI** mcrI haeIII/palI fnu4HI eael cfrI **b**BoFI acii bbvI mslI nlaIII fnu4HI bsoFI

mbol/ndell[dam-]

6401 ACAGAAAAGC ATCTTACGGA TGGCATGACA GTAAGAGAAT TATGCAGTGC TGCCATAACC ATGAGTGATA ACACTGCGGC CAACTTACTT CTGACAACGA TGTCTTTTCG TAGAATGCCT ACCGTACTGT CATTCTCTTA ATACGTCACG ACGGTATTGG TACTCACTAT TGTGACGCCG GTTGAATGAA GACTGTTGCT foki nlaiii BfaNI

mbol/ndell[dam-] alul hpall dpnII[dam-] bsaWI nlaiv dpnI[dam+] sau3AI mbol/ndell[dam-] Sau3AI maeIII dpnII(dam-) dpnI[dam+] nlaIII Bau96I avalI asuI

6501 TCGGAGGACC GAAGGAGCTA ACCGCTTTTT TGCACAACAT GGGGGATCAT GTAACTCGCC TTGATCGTTG GGAACCGGAG CTGAATGAAG CCATACCAAA AGCCTCCTGG CTTCCTCGAT TGGCGAAAAA ACGTGTTGTA CCCCCTAGTA CATTGAGCGG AACTAGCAAC CCTTGGCCTC GACTTACTTC GGTATGGTTT acil aluI mnlI

nlalli alwi[dam-]

FIG. 481

			tru91	mseI	asel/asnl/vspl	ACANTINATA	TGTTAATTAT
msp1	hpall	I scrFI	ncil	dsaV	cauli	CITCCCGGCA	SAAGGGCCGT
		aluī	rmal	maeI	pfal	CTTACTCTAG (SAATGAGATC
			berl	tru91	mseI	TATTAAC TGGCGAACTA	ATAATIG ACCGCTIGAT
hinPI	hha I/cfoI	mstI	avill/fspl	maell	psp1406I	A ACGITCCCCA AAC	T TGCAACGCGT TTG
		fnudHI	baoFi	TOTAL PREDI	fact the transfer	A TROUBLE BOOK ANTERCANC	GCTGCTCGCA CTGTGGTGCT ACGGTCGTCG TTACCGTTGT TGCAACGCGT TTGATAATTG ACCGCTTGAT GAATGAGATC GAAGGGCCGT TGTTAATTAT
				T am	INCO INCO INCOM	ATGGTACON ANCINCACTA CITACTOR ANTGGCAACA ACGTTGCGCA AACTATTAAC TGGCGAACTA CTTACTCTAG CTTCCCGGCA ACAATTAATA	GCTGCTCGCA CTGTGGTGC

Idsm

bsmAI bsal 6701 GACTGGATGG AGGCGGGATAA AGTTGCAGGA CCACTTCTGC GCTCGCCCCT TCCGGCTGGC TGGTTAATG CTGATAAATC TGGAGCCGGT GAGCGTGGGT CIGACCIACE ICEGECIAIT ICAACGICEI GGIGAAGACG CGAGEEGGGA AGGEEGAEGG ACCAAAIAAC GACIAITIAG ACCIEGGECA CICGCACECA cfr101/bsrFI bpmI/gsuI{dcm-} nlalv hphI hpall cacel hpall Idsm haeIII/palI .. sau96I hinpi asui hha1/cfoI Bau96I avall asul acil mnll fokI bsrl

bgll

Idsm

6801 CTCGCGGIAT CATTGCAGCA CTGGGGCCAG ATGGTAAGCC CTCCCGTATC GTAGTTATCT ACACGACGGG GAGTCAGGCA ACTATGGATG AACGAAATAG GAGCGCGCATA GTAACGTCGT GACCCCGGT TACCATTCG GAGGGCATAAC TGCTTTATC fokI ahdI/eam1105I hinfI mn]I haeIII/palI 196nes nlaiv berl asul fnu4HI bsoFI bbvI bsh1236I berDI funDII/mvnI acil betul thal

tru91 6901 ACAGATCGCT GAGATAGGTG CCTCACTGAT TAAGCATTGG TAACTGTCAG ACCAAGTTTA CTCATATATA CTTTAGATTG ATTTAAAACT TCATTTTAA TGTCTAGGGA CTCTATCCAC GGAGTGACTA ATTCGTAACC ATTGACAGTC TGGTTCAAAT GAGTATATAT GAAATCTAAC TAAATTTTGA AGTAAAATT mBeI ahalll/dral tru9I meeI maelll tru9I mseI dpnI[dam+] hglCI
dpnII[dam-] banI mnlI nlaIV mpol/ndell[dam-] ddeI Bau3AI

mbol/ndell[dam-] dpnII[dam-] dpnI[dam+] Bau3AI 7001 ITTAAAAGGA TCTAGGIGAA GAICCITIII GAIAAICICA IGACCAAAAT CCCITAACGI GAGIITICGI ICCACIGAGC GICAGACCCC GIAGAAAAGA AAATTITCCI AGAICCACII CIAGGAAAAA CIAIIAGAGI ACIGGIIIIA GGGAAIIGCA CICAAAAAGCA AGGIGACICG CAGICIGGGG CAICIIIICI hgal maell tru91 mecI nlaIII bspHI rcal mbol/ndeII[dam-] dpnII[dam-] dpnI[dam+] alwi[dam-] bstYI/xhoII ahaili/drai bfai mboli[dam-] 8au3AI mbol/ndeII [dam-] sau3AI hphI dpnII (dam-) tru9I betYI/xhoII dpnI[dam+] alwI[dam-] rma I maeI mseI

FIG. 48V

	Sausat	mpol/ndell[dam-]	dpnI[dam+]	dpnII dam-	alwI [dam-]		hpall alul	GTTTGTTTGC CGGATCAGA	CAAACAAACG GCCTAGTTCT
						acli	nspBII	ACCAGCGGTG	TGGTC3CCAC
							acii	NACCACCCCT	TTGGTGGCGA
								CMACMAM	GTTTGTTTT
			ını	cacel	fnu4HI	bsoFI	bbvI	CTGCTGCTTG	GACGACGAAC
		-] thal	fnuDII/mvnI	bstul	bsh1236I	hinPI	hhal/cfof bbvl	TGCGCGTAAT	ACGCGCATTA
sau3AI	mboli[dam-]	sau3AI mbol/ndell[dam-]	I	dpn[dam+] dpn[dam+]	donlidam-1 donlidam-1	betyl/xholl alwI[dam-]	alwi[dam-] bstXI/xhoII	7101 TCANAGGATC TICTIGAGAT CCTITITIC TGCGCGTAAT CTGCTGCTTG CAAACAAAA AACCACCGCT ACCAGGGGTG GTITGTITGC CGGATCAAGA	AGITICCIAG AAGAACICIA GGAAAAAAA ACGCGCATIA GACGACGAAC GIIIGIIIII TIGGIGGCGA IGGICGCAC CAAACAAACG GCCIAGIICI

haeIII/palI	bslI hael	7201 GCINCCNACT CTITITCGA AGGINACTGG CTTCAGCAGA GCGCAGATAC CANATACTGT CCTTCTAGTG TAGCCGTAGT TAGGCCACCA CTTCAAGAAC CGAIGGIIGA GAMAAAGGCI ICCATIGACC GAAGICGICT CGCGTCIAIG GTTIATGACA GCAAGAICAC ATCGGCATCA ATCCGGIGGI GAAGIICTIG
macI	bfal	CCTTCTAGTG TAG GCAAGATCAC ATG
hinpi	hha1/cfo1	SCGCAGATAC CAAATACTGT SGCGTCTATG GTTTATGACA
bsrI	maeIII eco57I }	STANCTEG CTTCAGCAGA CONTINUES CANTIGACE GANGTEGTET (
	E	7201 GCTACCAACT CTTTTTCCGA AGG CGATGGTTGA GAAAAAGGCT TCC

rmal

F C 1	BCIFI	ncil	Idsm	hpall	dsav pleI	cauli hinfi	CCTCTCTTAC CGGGTTGGAC TCAAGACGAT GCACAGAATG GCCCAACCTG AGTTCTGCTA
fnutHI	DSOF1	bbvI	fnu4HI	alwni [dcm-]	bsrI bsoFI	and I maelli bbvi bsri	SCTACATA CCTCGCTCTG CTAATCCTGT TACCAGT

лагри	96	7		alw441/snol alul ddel
				hhal/cfol alw441,
				maelli

7401 AGTTACCGGA TAAGGCGCAG CGGTCGGGCT GAACGGGGG TTCGTGCACA CAGCCCAGCT TGGAGCGAAC GACCTACACC GAACTGAGAT ACCTACAGG TCAATGGCCT ATTCCGCGTC GCCAGCCCGA CTTGCCCCCC AAGCACGTGT GTCGGGTCGA ACCTCGCTTG CTGGATGTGG CTTGACTCTA TGGATGTCGC

FIG. 48W

deav betNI beaJI aluI apyI[dcm+] sGAGCTTCCA	
baasi hinpi mnli hhal/cfoi sagga agggacaag gg	
mspl hpall fnu4Hl bsll bsoFl saWl acll cccggrAAG CGGCAGGGTC GGAAC	
mspl hpall bsll l bsawl GACAGGT ATCCGGT/ CTGTCCA TAGGCCA/	
mspl hinpi halveld hbalveld segretteer hbalveld hbalveld shorteere generaged gegenered generale generate generate generale erectered hcecareace cerecans corrected hcecareace cerecans corrected hbalveld	SCRFI NVAI

ecoRII

SCLFI IDVE

		;	ATOTU
			tagI
T W A T	ecoRII	dsav	Po+NT

Bfani 3T GATGCTCGTC AGGGGGCGG AGCCTATGGA 2A CTACGAGCAG TCCCCCGCC TCGGATACCT	tf1I hinf1	CC TGCGTTATCC CCTGATTCTG TGGATAACCG
apyl(dcm+) Apyl(dcm+) Apyl(dcm+) ACCTATES CATATITE GCACCTAT GCACATATAGA AGCATATAGA CCCCATAGA GACATAGA ANTATAGA CAGCCCAAAG CGATGAGAC TGAACTCGCA GCAAAAACA CTACGAGACAG TCCCCCGCC TCGATACCT CCCCCTTGC GGACCATAGA ANTATCAGGA CAGCCCAAAG CGGTGGAGAC TGAACTCGCA GCTAAAAAACA CTACGAGCAG TCCCCCCGCC TCGGATACCT	hacII/pall scrFI mval bsli ecoRII dsav hacIII/pall nspI apyI[dcm+] haeI nspHI	CCT TTTGCTC GGA AAACGAG
Apyl(dem+) 7601 GGGGGAAACG CCTGGTATCT TTATAGTCCT CCCCCTTTGC GGACCATAGA AATATCAGGA	haeIII/pali fnu4HI bsoFI acii thai bsli fnuDII/mvni bstUI	CACHI DENIZION NIA 7701 AAAACGCCAG CAACGCGGCC TITITACGGT TITIGGGGTC GTIGCGCCGG AAAAATGCCA

mboll hhal/cfol earI/ksp632I sapi hinPi haell acti mnlI bbvI pleI hinPI hinfI hhal/cfol fnu4HI bsoFI bsiEI fnu4HI bsoFI bbvI barBI fnu4HI bsoFI cac81 ac11 acll aluI

7801 TATTACCGCC TITGAGIGAG CIGATACCGC TCGCCCCAGC CGAACGACCG AGCGCAGCGA GICAGIGAGC GAGGAAGCGG AAGAGCGCCC AATACGCAAA ATAATGGCGG AAACTCACTC GACTATGGCG AGCGGCGTCG GCTTGCTGGC TCGCGTCGCT CAGTCACTCG CTCCTTCGCC TTCTCGCGGG TTATGCGTTT

FIG. 48X

maellI hhal/cfol asel/asnl/vspl 7901 CCGCCTCTCC CCGCGCGTTG GCCGATTCAT TAATCCACCT GGCACACAG GTTTCCGGAC TGGAAAGCGG GCAGTGAGCG CNACGCAATT AATGTGAGTT GGCGCAGAAGG GGCGCGCAAC CGGCTAAGTA ATTAGGTCGA CCGTGCTCAA ACTAGGTCGA CCATTCGCC CGTCACTCGC GTTGCGTTAA TTACACTCAA 8001 ACCICACICA TIAGGCACCC CAGGCITIAC ACTITATGCI TCCGGCTCGT ATGITGTGTG GAATIGTGAG CGGATAACAA TITCACACAG GAAACAGCTA tru9I mseI hinPI berBI cacel acil bsrIhpaII mspI cfrI hinfI mseI nspBII eael tfil asel/asnl/vspl tru91 pvull aluI bstUI haeIII/pall hgici apyi [dcm+] ecoRII scrFI nlaIV bstNI dsav banl baaJI IBVE bsh1236I ball acii mnll

cacel

funDII/mvnI

hhal/cfol

thal

hinPI

fnuDII/mvnI

bsh1236I

betui thaI

FIG. 48Y

TGGAGTGAGT AATCCGTGGG GTCCGAAATG TGAAATACGA AGGCCGAGCA TACAACACAC CTTAACACTC GCCTATTGTT AAAGTGTGTC CTTTGTCGAT

BIOI TGACCATGAT TACGATTAA (SEQ IO NO: 68) ACTGGTACTA ATGCTTAATT

asp700 Iumx

nlalil

asel/asnl/vspl

tru9I

mseI

FIG. 48Z

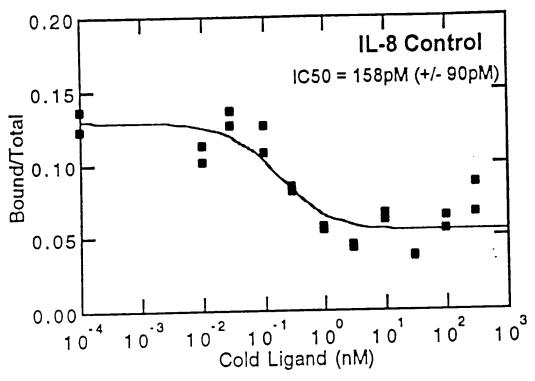


FIG. 49A

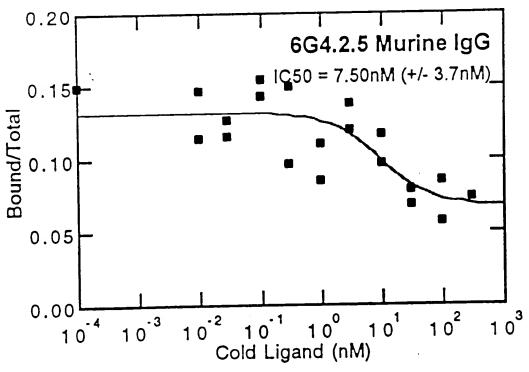


FIG. 49B

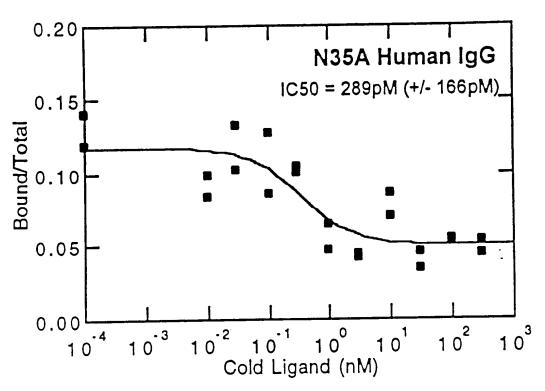


FIG. 49C

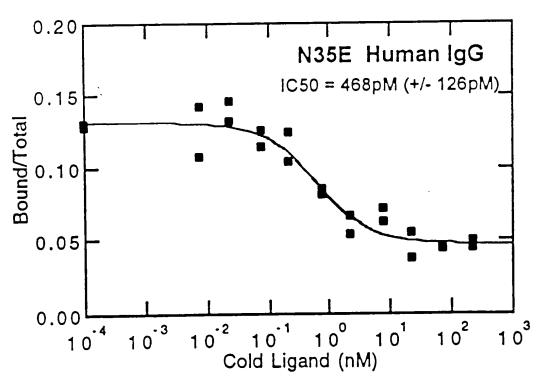


FIG. 49D

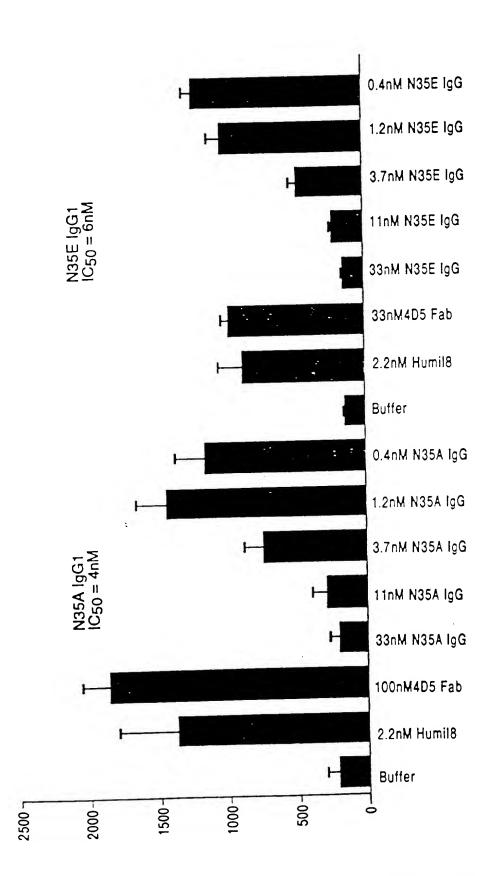
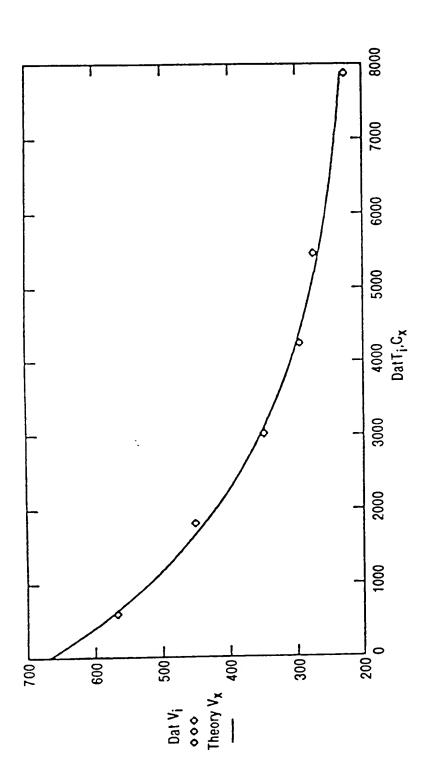


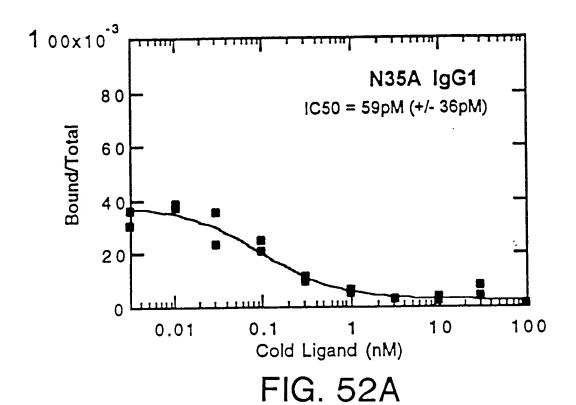
FIG. 50A

FIG. 50B



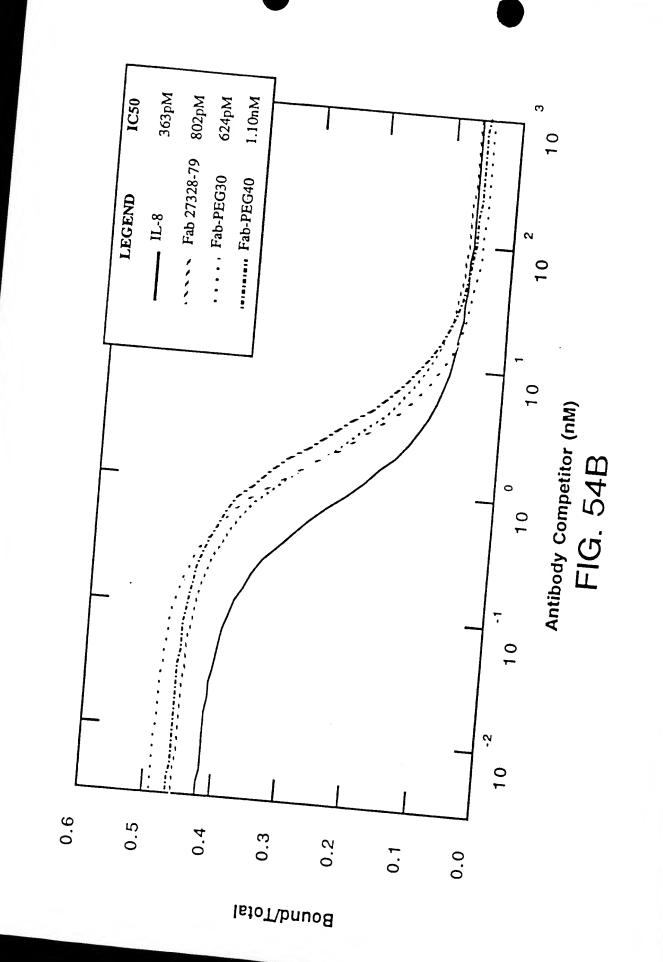
Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.IgG1

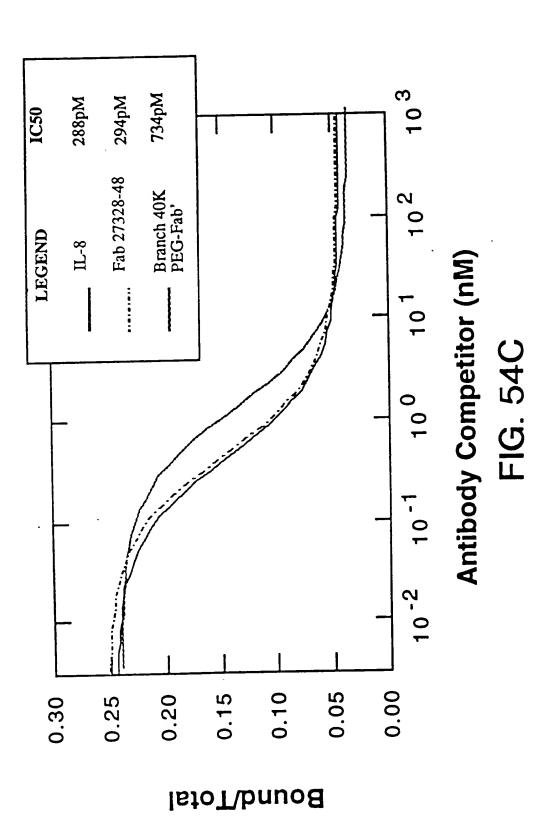
MPLE	ka	kd	Kd	r
Murine 6G4.2.5 IgG2a	8.3x105	2.9×10^{-4}	350pM	
6G4V11N35A-IgG1	8.7×10^{5}	$7.7x10^{-5}$	88pM	\ \(\)
6G4V11N35E-IgG1	3.0×10^{6}	1.4×10^{-4}	49pM] FIG. 51

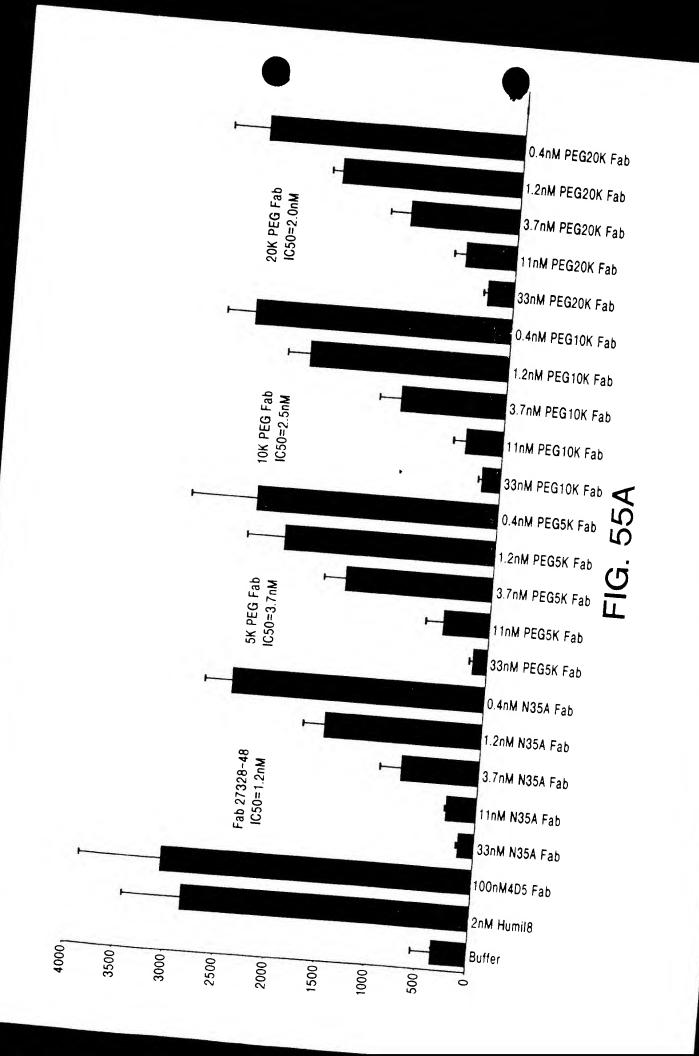


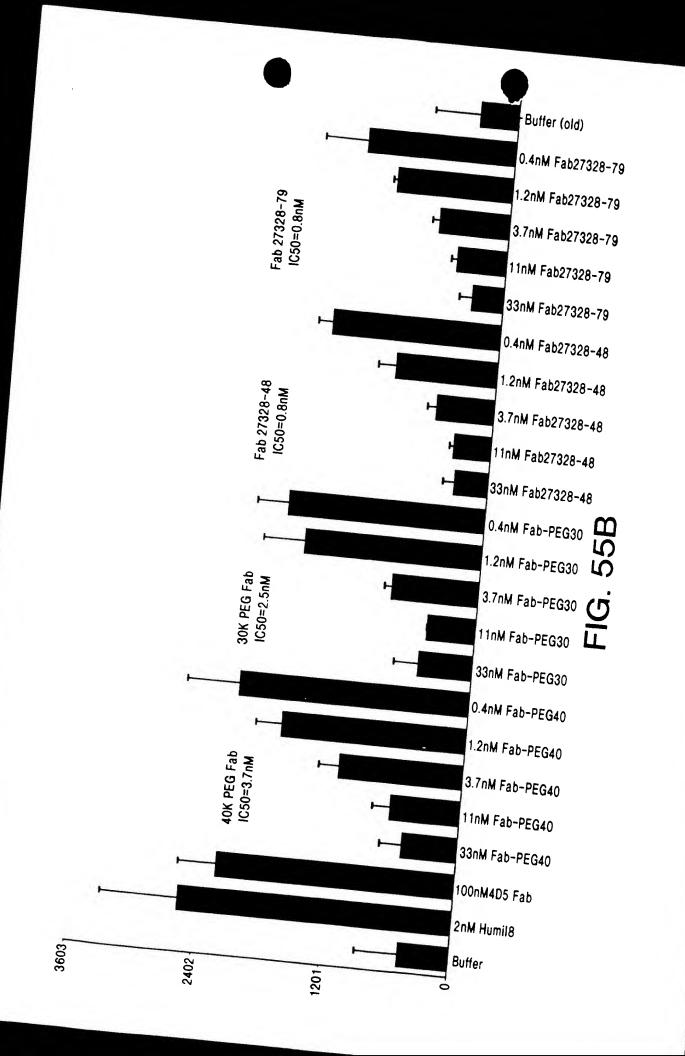
N35E IgG1 80 IC50 = 19pM (+/- 15pM) 0.01 0.1 1 10 100 Cold Ligand (nM) FIG. 52B

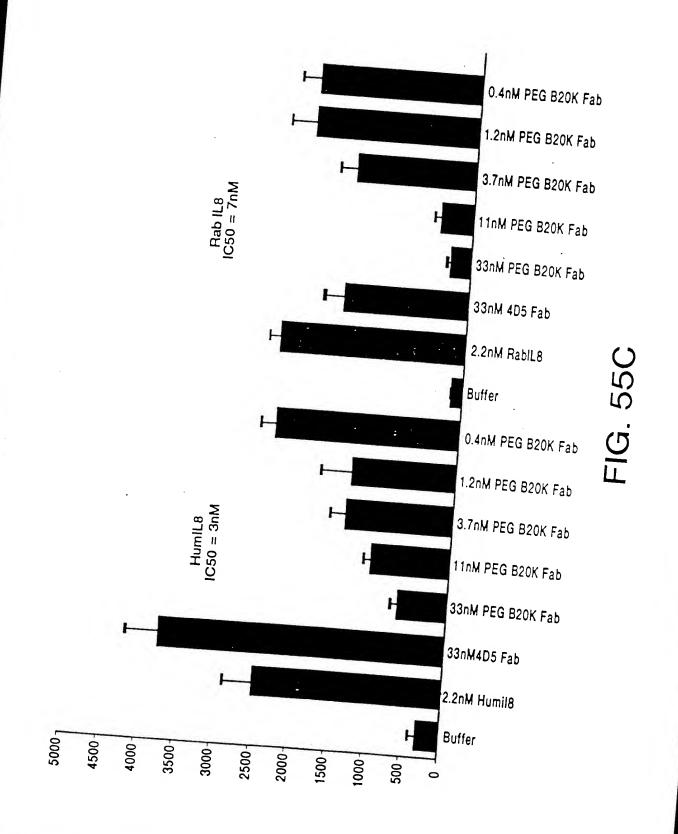
781	AAA	AAG(GGT	AΤ	CTAG	AGG	TTG	AGG	TGA	TTTT	ATY	GAA	AAAG	A A	TAT	CGC.	ATT	TCT	JCT.	IGCA ACGT
	TT.	MC	CCA'	ΓA	GATC	TCC	AAC	TCC.	ACT	AAAA	TA	CTT.	K I	r T J	ATA T	GCG.	F	AGA.	L	A
-1											M	V	Λ.	.1	_	^	•	_	_	
0/1	m~r	ארח עים	ململت	CG	Lalalal	ملعلد	ጥልጥ	TGC	TAC	AAAC	GC	GTA	CGCT	3 A	GGT	TCA	GCT	AGT	GCA	STCT
	ACI	ልጥል	ממר	C	AAAA	AAG	ATA	ACG	ATG	TTTG	CG	CAT	GCGA(CI	CCA	AGT	CGA	TCA	CGI	CAGA
-11	S	М	F	v	F	s	I	A	T	N	A	Y	A I	Ε	V	Q	L	V	Q	S
901	GG	CGG'	TGG	CC	TGGI	GCA	GCC	AGG	GGG	CTCA	CT	CCG'	TTIG'	rc	CIG	TGC	AGC TCC	JIC	7.CC	STAC
_	CCC	GCC.	ACC	GG	ACCA	CGT	CCC	TCC	CCC	GAGT S	GA	رياني ح	AAAC	4. G	CAC	ACG A	A .	S	G	Y
8	G	G	G	L	٧	Q	P	G	G	3	ם	K	ш.	,	•	••	••	_		
0.61	m~ (ىلغات	~m~	C A	CTC N	ርሞኔ	ጥልጥ	GCA	CTG	GGTC	CG	TCA	GGCC	c c	:GGG	TAA	GGG	CCT	GGA	ATGG
	AC	222	GAG	CT	CAGT	GAT	ATA	CGT	GAC	CCAG	GC	AGT	CCGG	G G	CCC	ATT	CCC	GGA	CC1	TACC
28	s	F	S	s	Н	Y	М	_H	W	V	R	Q	A	P	G	K	G	L	E	W
1021	GT	IGG.	ATA'	TA	TTGA	TCC	TTC	CAA	TGG	TGAA	AC	TAC	GTAT.	A A	TCA	AAA	GTT	CAA	GGG	CCGT
	CA	ACC	TAT.	AΤ	AACI	`AGG	AAG	GTT	ACC	ACTT	TG	ATG	CATA	тт	AGI	-I-I-I	CAA	GIT	666	GGCA D
48	V	G	<u>Y_</u>	_I_	D_	Р_	S	<u>N</u>	<u> </u>	E	T	<u>T</u>	_Y	И					<u> </u>	Λ.
								000	~		20	200	እመአር	с п	70C N	CAT	443	CAG	ССТ	GCGT
1081	TT	CAC	TTT.	AT T	CTCG	CGA	CAA	CIC	CAA	TTTG	AC TC	MGC.	ለ፤ አር ጥልጥር		CGT	СТА СТА	CTT	GTC	GGA	CGCA
69	AA	an Te	AAA' T.	TA	GAGC R	.GC I	N	S	K	N	T	A	Y	L L	Q	М	N	S	L	R
1141	GC	IGA	GGA	CA	CTGC	CGT	CTA	TTA	CTG	TGCA	ΑG	AGG	GGAT	T ?	TCC	CTA	CAA	TGG	TGA	CTGG
	CG	ልርጥ	CCM	GТ	GACG	GCA	GAT	AAT	GAC	ACGT	TC	TCC	CCTA	ΑJ	rage	GAT	GTT	ACC	ACT	GACC
88	Α	E	D	T	Α	V	Y	Y	С	A	R	<u>G</u>	_D	<u>Y_</u>	R_	<u> </u>	N	<u> </u>	<u> </u>	<u> </u>
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1201	TT	CTT	CGA	CG	TCTC	GGG	TCA	AGG	AAC	CCTG GGAC	G.T	CTC	CCIC	y (יככני	CIC	GTG	GTT	CCCG
100	AA(GAA	GCT	GC 77	AGAC	عات.	AGI	100	ጥ	L	V	T	v	s	S	A	S	T	K	G
100		_1_		<u> </u>	**	•	¥	Ū	•	_	·									
1261	CC	ATC	GGT	ст	TCCC	CCI	GGC	ACC	CTC	CTCC	AA	GAG	CACC	T	TGC	GGG	CAC	AGC	GGC	CCTG
	CC	ጥልር	CCA	CV.	ACCC	CGA	CCG	TGG	GAG	GAGG	TI	CTC	GTGG	A C	GACC	ccc	GTG	TCG	CCG	GGAC
128	P	S	V	F	P	L	A	P	S	S	K	S	T	S	G	G	T	A	Α	L
													~ ~ ~ ~	~ .	~~~~	· _ m-		CTC	· » ~ ~	
1321	GG	CTG	CCT	.GG	TCA	AGG	ACTA	CTI	222	CGAA GCTT	CC	GGT	CTCC	G 7	IGIC	CAC	CUAL YYYYY	GAG	.AGG	೧೦೦೦ ೧೦೧೧
1.40	CC	GAC	:GGA	CC	AGT.	ויטטיו	GAT.	GAA	الحاص	E	P	V	T	v	S	W	N	S	G	A
148	G	C	مر	٧	K	ט	•	•	•	_	•	•	_	•	_					
1381	СТ	GAC	CAG	CG	GCG	rgc#	ACAC	CTI	CCC	GGCT	GI	CCT	'ACAG	T (CTC	:AGG	ACT	CTA	CTC	CCTC
	CA	CTY:	יכידיכי	GC.	CGC	ACG	CTG	GAA	GGC	CCGA	CA	LGGA	TGTC	A (GAC	TCC	TGA	GAT	GAG	GGAG
168	L	T	S	G	V	Н	T	F	P	A	V	L	Q	S	S	G	L	Y	S	L
								om.		20100	mer	~~~	CACC	C 1	CAC	ירת א	С <u>а</u> т	CTC	ממר:	CCTC
1441	AG	CAG	CGI	YGG	TGAG	CCG'	rgcc	CIC	CAC	CAGC CGTCG	7.7		CACC	C /	TO AC	ת בינו	CTA CTA	GAC	CTT	GCAC
100	TC	GTC	:GCA	CC	ACT	لاساجاد 17	ACGG D	GAC	2	S	T.	G	T	0	T	Y	I	С	N	v
188	S	5	V	٧	1	•	F	5	٦	-	_	•	•	*	_	_				
1501	מ מ	.TYC 2	CAA	.GC	CCA	GCA	ACAC	CAZ	\GGT	rcgac	ΑZ	GAA	AGTT	G Z	AGCC	CAA	LATC	TTC	TGA	CAAA
	TAL	יא כים	لملاته	YC	CCTY	CIT	TGTG	GTT	CCZ	AGCTG	L	Σ TI	TCAA	C 1	ΓCGC	GTI	TAG	AAC	CACI	GIII
208	N	Н	K	P	s	N	T	K	V	D	K	K	V	E	P	K	S	С	D	K
1561	AC	TC	CAC	TA	GCC	CGC	CGTG	a C m	٤	ID NO:	0-1	'								
	TG	AGI	CTC	ATE	CGG()ئانئ ھ	JCAC ∩	1.	_	_,_		_								
228	T	Н	T	Ċ	(SE)	ም ዕነሰ:	ND: 7	107		=10	֝֡֡֞֞֞֞֞֞֞֞֞֞֞֡֡	5	3							
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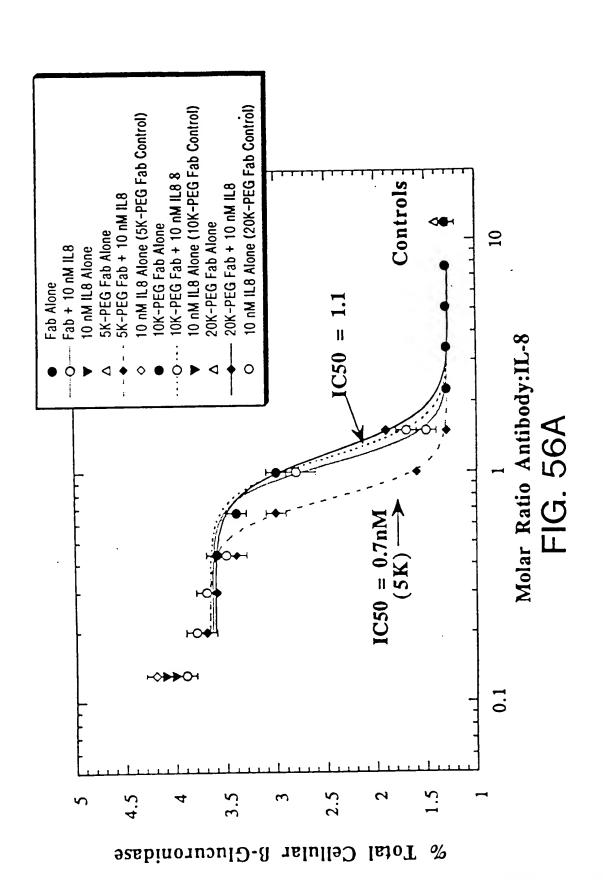


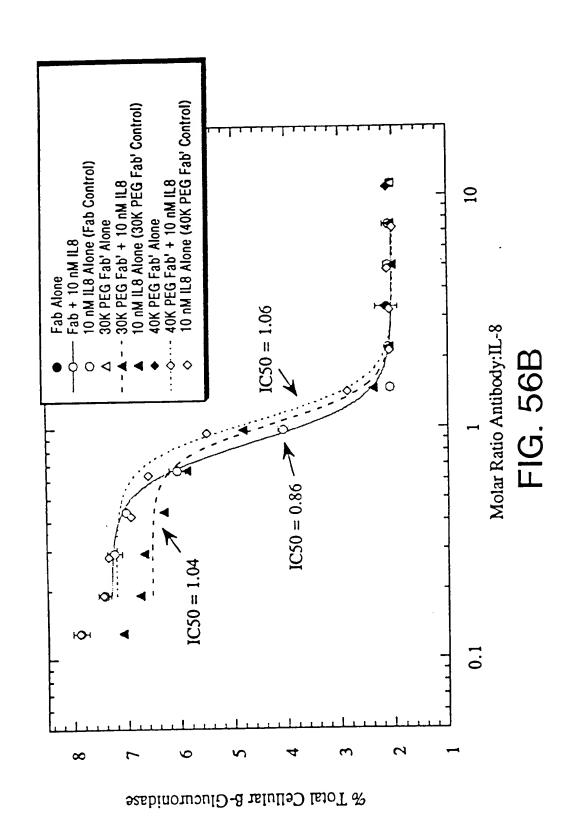




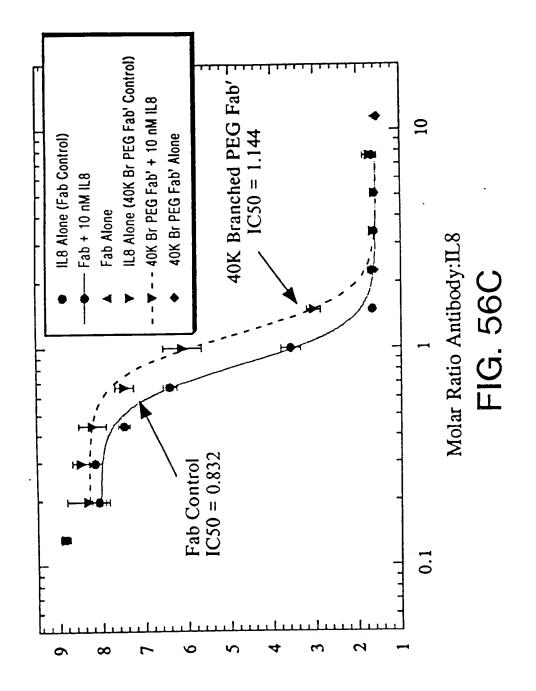


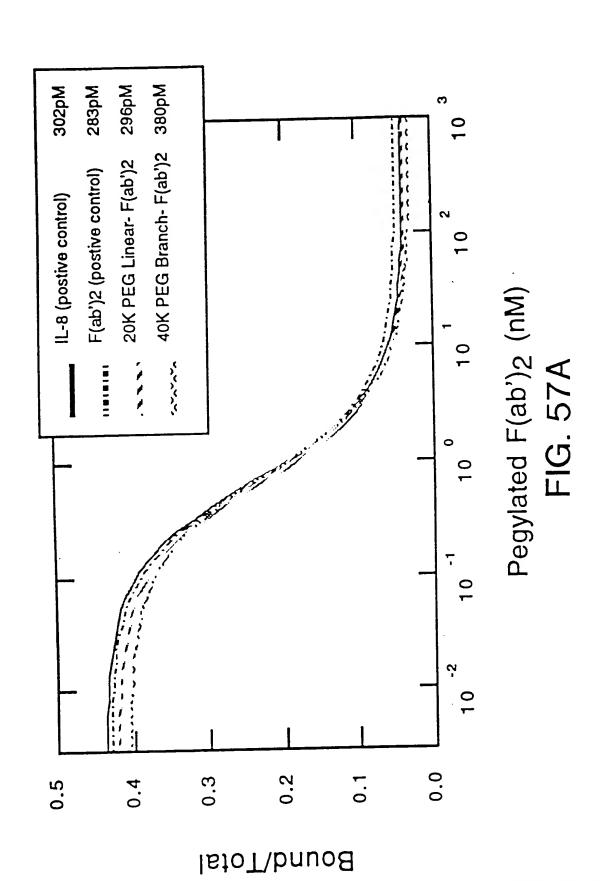


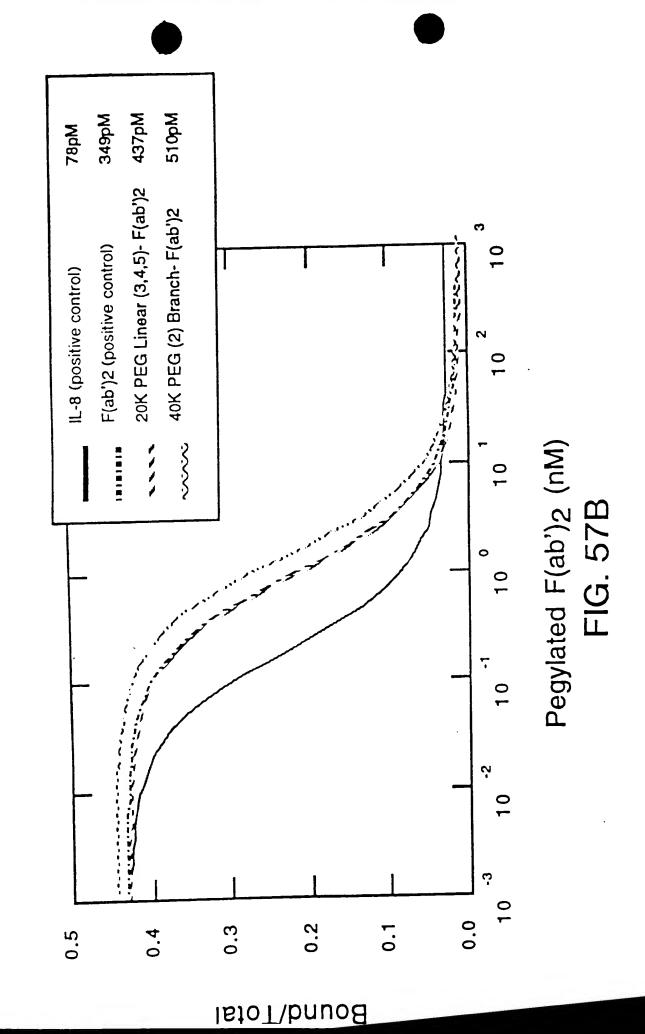


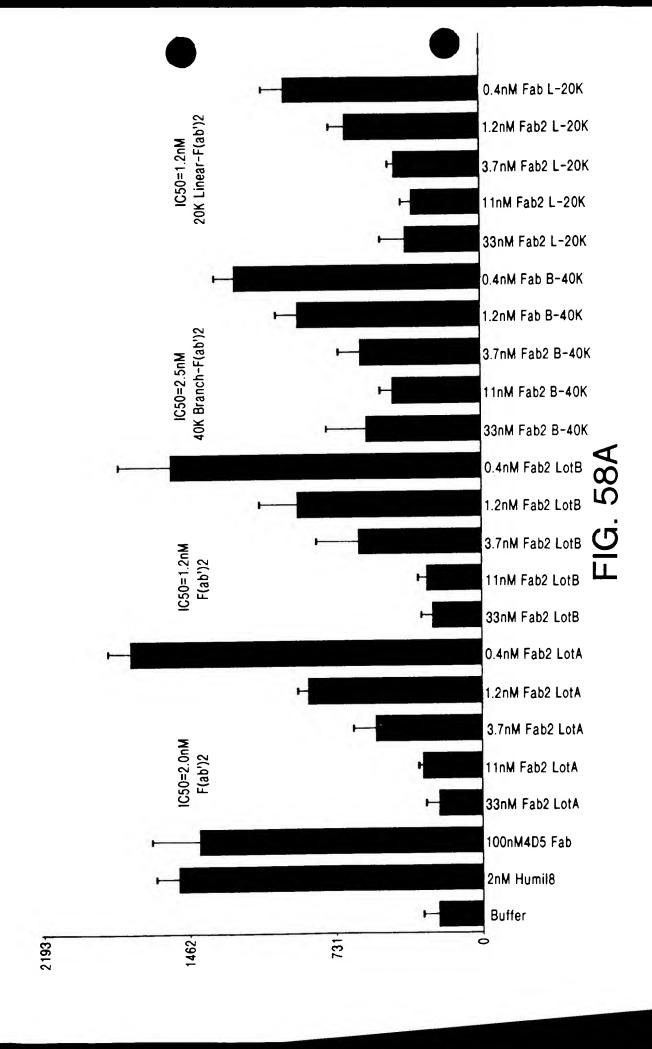


% Total Cellular B-Glucuronidase Activity









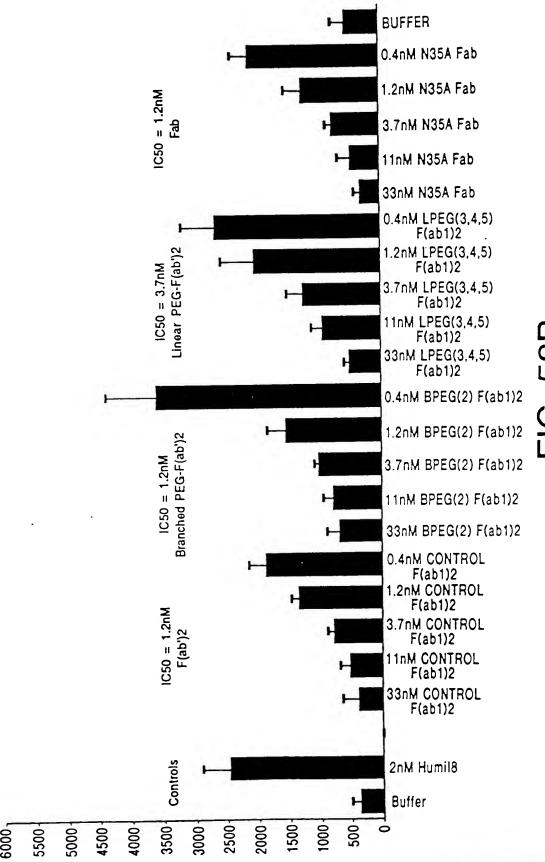
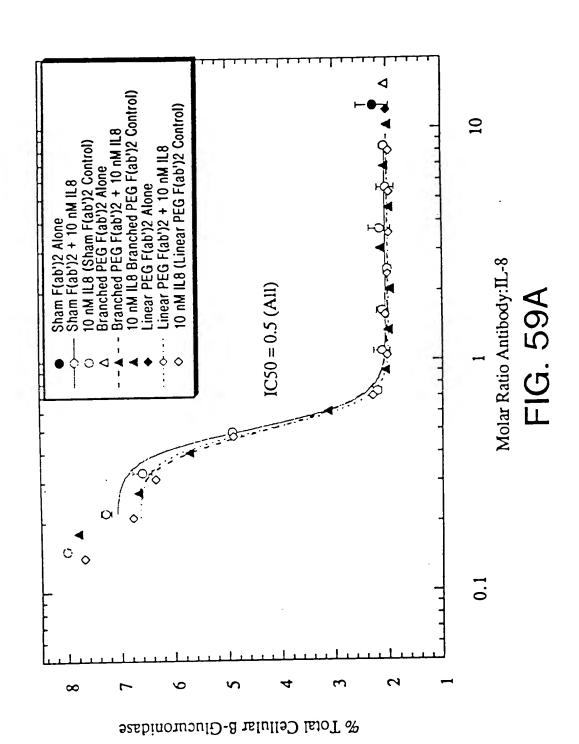
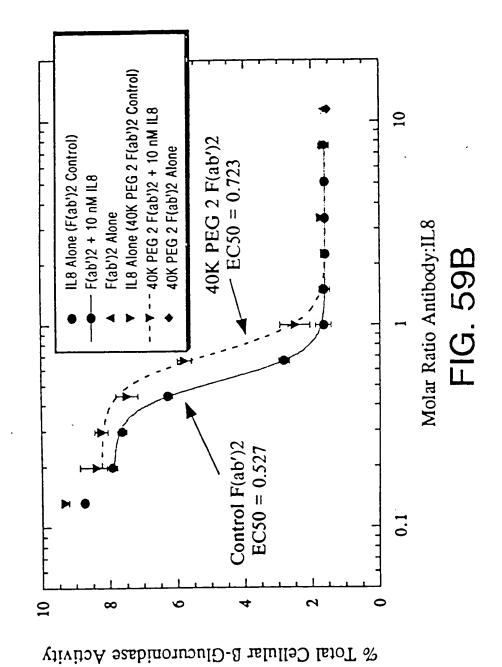
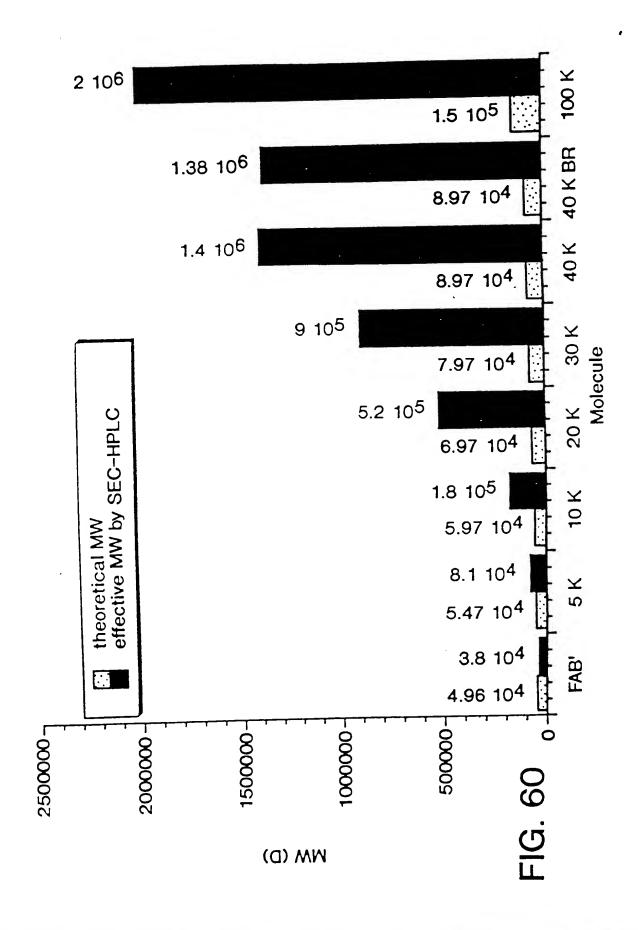
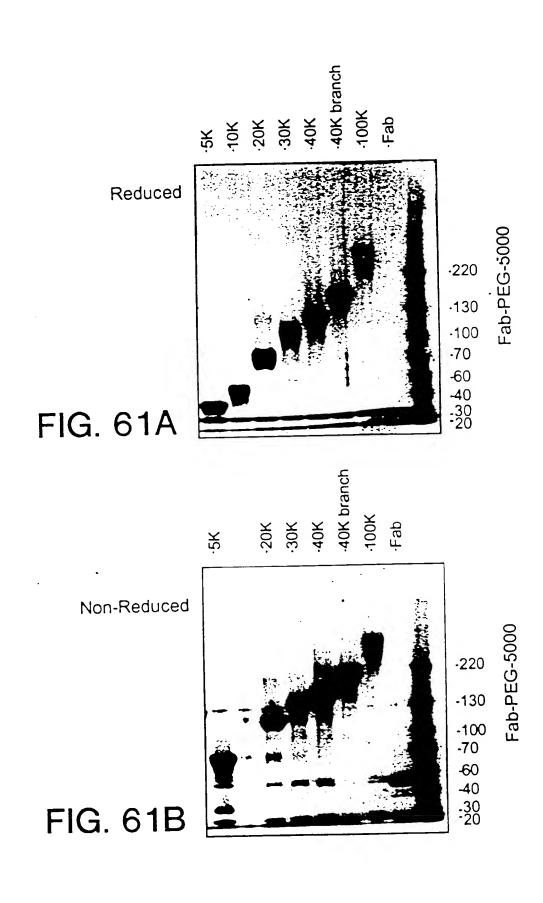


FIG. 58B









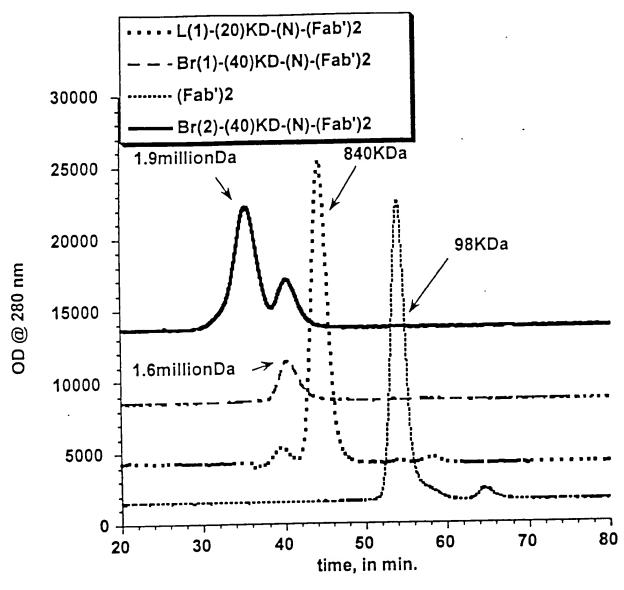


FIG. 62

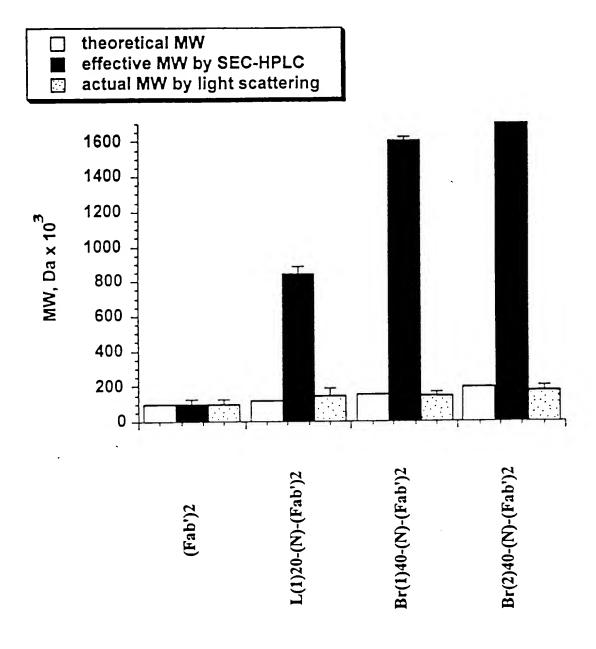


FIG. 63

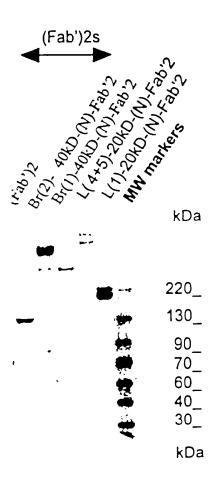
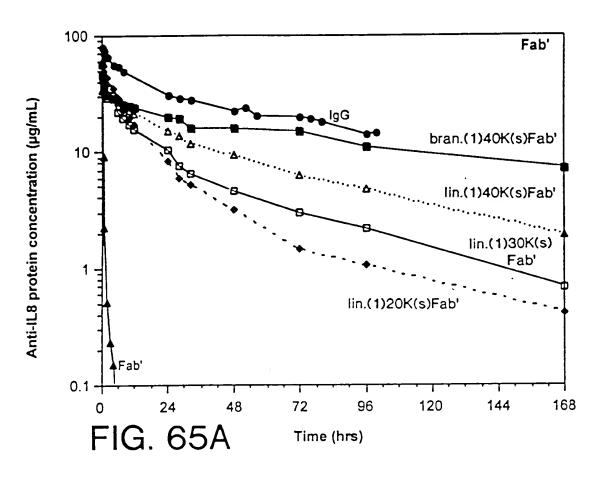
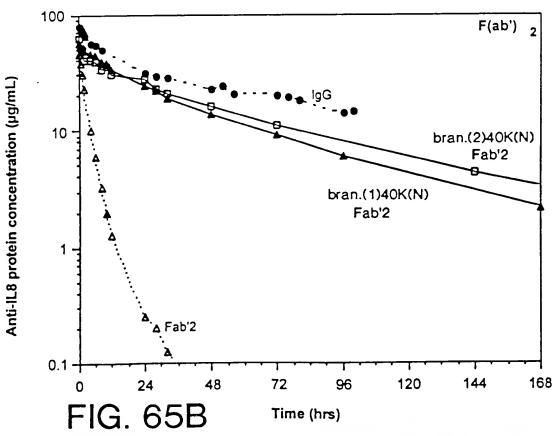


FIG. 64





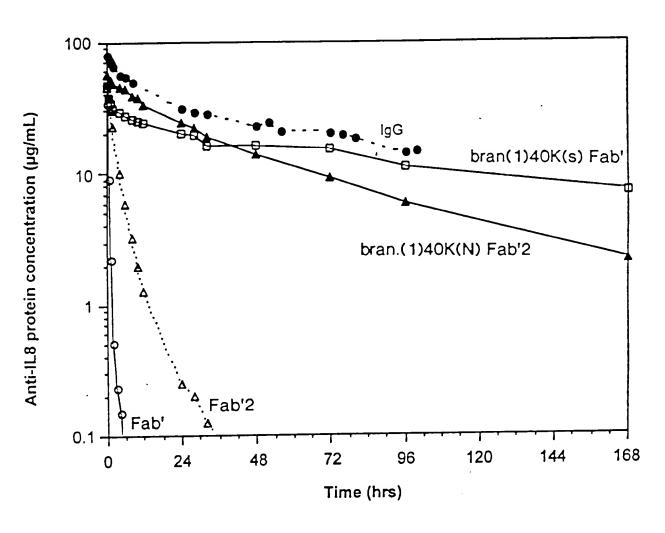
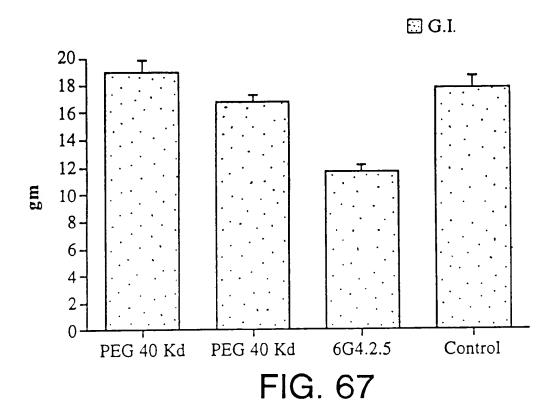
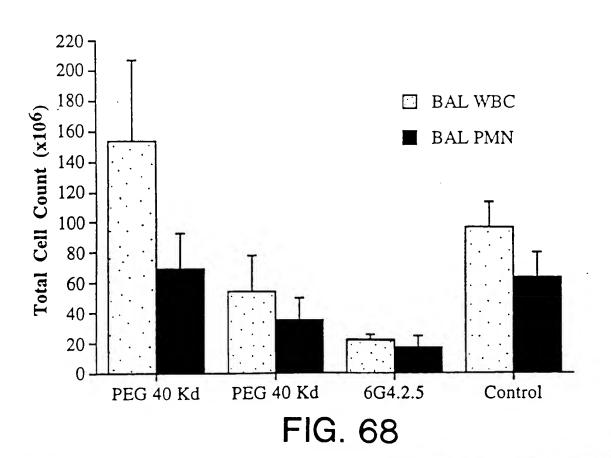


FIG. 66





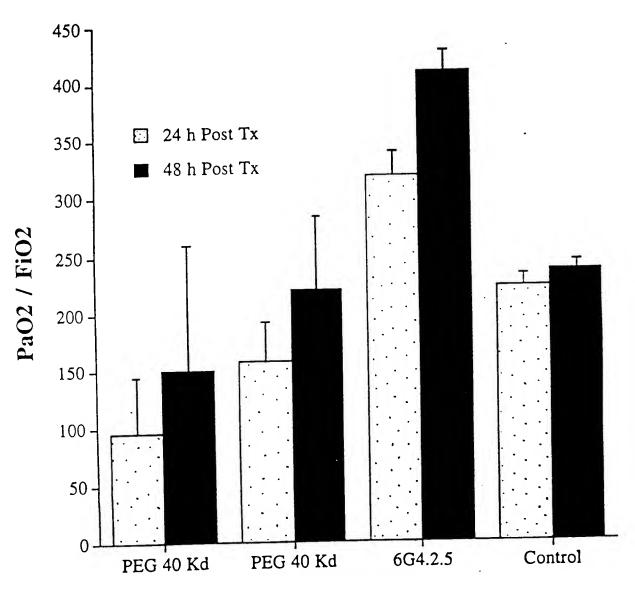


FIG. 69

Oxygenation in 100% O2 @24 h Post Anti-IL8 Tx 500 400 PaO2 (mmHg) 300 200 100 0 Peg40K-br Peg40K-br Saline Peg20K-lin 6 G 4 5 ml IV @-10' & 6 h (n=25) 20 mg/kg IV @-10' (n=2) 7 mg/kg IV @-10' & 6 h (n=5) 5 mg/kg IV @-10' (n=7) 5 mg/kg IV @-10' (n=3)

Oxygenation in 100% O2 @48 h post Anti-IL8 Tx 500 400 PaO2 (mmHg) 300 200 100 0. Peg40K-br Peg40K-br Saline Peg20K-lin 6 G 4 20 mg/kg IV @-10' (n=2) 5 ml IV @-10' & 6 h (n=16) 5 mg/kg IV @-10' 5 mg/kg IV @-10' 7 mg/kg IV @-10' & 6 h (n=5)

(n=3)

(n=7)

Gross Lung Weight to Body Weight Ratio 8 7 6 5 4 3 2 1 1 0 Peg20K-lin 6G4 Peg40K-br Peg40K-br Saline

5 mg/kg IV @-10' (n=3) 20 mg/kg IV @-10' (n=3) 5 ml IV @-10' & 6 h

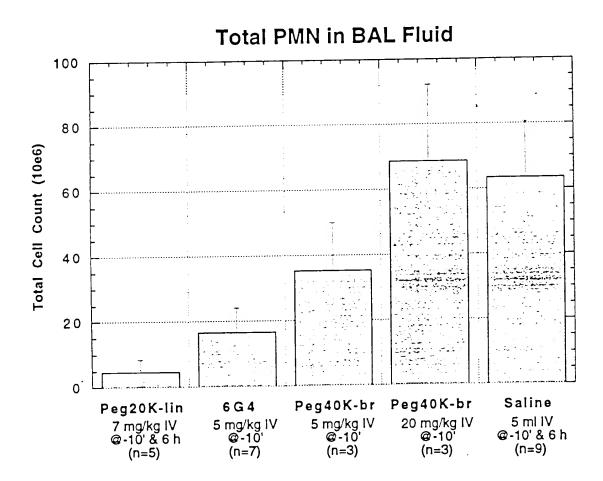
(n=29)

GLW / BW Ratio

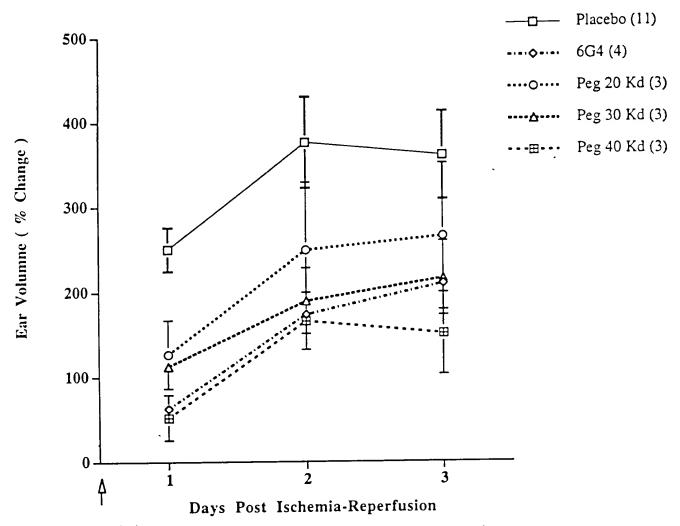
7 mg/kg IV @-10' & 6 h (n=5) 5 mg/kg IV @-10'

(n=7)

Total WBC in BAL Fluid 200 150 Total Cell Count (10e6) 100 50 0, Peg40K-br Saline Peg40K-br 6 G 4 Peg20K-lin 5 ml IV @-10' & 6 h (n=11) 20 mg/kg IV @-10' (n=3) 5 mg/kg IV @-10' (n=3) 7 mg/kg IV @-10' & 6 h (n=5) 5 mg/kg IV @-10' (n=7)



The Effect of Pegylated Anti-IL-8 in the Rabbit Ear model of Ischemia-Reperfusion Injury



Anti-IL-8 formulations: Single Dose (5 mg/kg) administered IV at time of reperfusion